

Antibiotic-impregnated PMMA hip spacers

Current status

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ABSTRACT The infection rate after primary hip arthroplasty lies at 1–2%. In the past few years, a two-stage protocol with the implantation of an antibiotic-loaded spacer has become a popular procedure in the treatment of infected hip joint arthroplasties. In this review, we pay special attention to the elution characteristics of the spacers, their mechanical stability and the clinical response. We conclude that hip spacers are an effective method in the treatment of hip joint infections, with success rates of over 90%.

The infection rate after total hip arthroplasty lies at 0.5–1.4% (Haaker et al. 2004). The use of antibiotic-impregnated polymethylmethacrylate (PMMA) interim prostheses/spacers has become a widespread technique in the treatment of postoperative infections after total hip arthroplasty, with success rates of over 90% (Younger et al. 1997, Koo et al. 2001, Takahira et al. 2003). The benefits of this method are (i) immediate treatment of the source of infection by reaching high antibiotic levels locally, (ii) maintenance of joint mobility, (iii) limitation of scar formation, (iv) absence of soft tissue contraction (otherwise usually resulting in leg length discrepancy), and (v) ease of re-implantation.

An important issue in the use of antibiotic-loaded spacers is the impregnation of bone cement. Not every antibiotic qualifies equally for incorporation into bone cement. Desirable characteristics

include: availability in powder form, wide antibacterial spectrum, bactericidity 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 (Murray 1984, Wahlig 1987). Aminoglycosides and glycopeptides are known to be the two groups of antibiotics that fulfill most of these criteria (Wahlig 1987).

Unfortunately, the recent increase in the number of antibiotic-resistant bacterial strains (Neu 1992, Cercenado et al. 1996, Krcmery et al. 1996, Wendt 1998) requires an adequate treatment strategy in order to avoid failures and multiple surgical interventions. Thus, although an antibiogram might be useful, it is not always helpful since some of the recommended antibiotics are inactivated just by mixing with the cement, or during its polymerization process (Buchholz and Engelbrecht 1970, Ger et al. 1977). Also, a low degree of antibiotic release from the cement might limit its application.

Currently, there are no established standards or clinical guidelines available for the treatment of the infected hip joint. This review covers present-day experience with antibiotic-loaded hip spacers in the treatment of hip joint infections. Specific attention is paid here to the incidence of complications and to the balance between mechanical stability and the elution characteristics of antibiotics.

One- or two-stage procedure?

Several methods of treatment can be chosen,

including a one-stage procedure, a two-stage procedure with a PMMA spacer, or a resection exchange arthroplasty/Girdlestone procedure (Wagner and Wagner 1995, Joseph et al. 2003). Before making a decision, the acuteness or chronicity of the infection, the type of infecting organism, its antibiotic sensitivity profile, its ability to manufacture glyco-calyx, the occurrence of severe soft-tissue damage and the extent of bone loss must be considered.

A two-stage approach permits identification of the infecting organism, determination of antibiotic sensitivity, and appropriate adjustment of antibiotic therapy before reimplantation. An adequate debridement of necrotic or infected tissues and removal of cement plus a greater flexibility in reconstructive options are also advantageous. However, the prolonged hospitalization and its associated costs, the delayed mobilization and rehabilitation, and the risk of additional surgery may be a drawback—especially in elderly patients.

Several studies have compared one-stage and two-stage procedures. Ure et al. (1998) emphasized that a direct exchange arthroplasty can only be carried out in early infections if the patient is not immunocompromized, if the infecting organism is of low virulence (no methicillin-resistant or gram-negative bacteria), if the surgeon is experienced, and if there are no major skin, soft-tissue or existing osseous defects. Delayed reimplantation procedures after a Girdlestone procedure are technically demanding due to scar formation, leg shortening, osteoporosis from disuse, and the distorted anatomy, and have thus been replaced by the implantation of spacers (Leunig et al. 1998).

Inclusion of studies

Data from 30 studies (26 in vivo, 4 in vitro) are presented. The studies were chosen after a Medline search (search words: hip infection, spacer(s), antibiotic-loaded) and after searching through the reference lists of the articles resulting from the Medline search. When there was more than one article published by the same author or group, the more relevant and/or recent paper was included. At least 316 hips have been treated by implanting an interim prosthesis. (Note that not every published study offers detailed data on the number of patients or hips treated). An infected total hip arthroplasty (THA) was the indication in most cases, followed

by septic arthritis. In the in-vitro test studies, the static strength, the elution of antibiotics and the surface-release relation were evaluated. The clinical studies concentrated on the outcome and complications.

Construction of antibiotic-loaded hip spacers

Table 1 shows manufacturing details of the spacers. Hand-formed prostheses have been used in 13 studies while standardized prostheses were used in 22 studies (4 of which were PROSTALAC (prosthesis of antibiotic-loaded acrylic cement)). Most spacers function as a hemiarthroplasty, whereas only a few offer the advantages of a THA (PROSTALAC and Hsieh et al. 2004). Almost half of the studies reported fixation of the spacer by cementation to the proximal part of the femur, and the other half used snap-fit as the method of fixation.

Unfortunately, there has been no study comparing the clinical performance and the complications associated with spacers with respect to their articulation and the fixation method. Although a proximal cementation of the spacer to the femur might preserve leg length and prevent any rotation, no study has demonstrated which one of the two methods is best. Moreover, THA-like spacers may improve the congruence of the joint compared to hemiarthroplasty-like ones, but there have been no reports investigating whether clinical performance is better with THA-like spacers.

The majority of studies have used Palacos bone cement. Cephalosporins, penicillin G, aminoglycosides and glycopeptides have been added to the cement, the two latter being used most often. While 25 spacers had mechanical support from metallic components, 7 spacers only consisted of antibiotic-impregnated cement.

Diagnostic steps

Many authors have emphasized the value of clinical history and physical examination, radiological evaluation and laboratory data, including C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and leukocyte blood account in confirming the diagnosis (Koo et al. 2001, Takahira et al. 2003, Durbhakula et al. 2004, Hsieh et al. 2005). An ESR of > 30–40 mm/h combined with a CRP level of > 10–20 mg/L is considered highly suggestive of infection (Durbhakula et al. 2004, Hsieh

Table 1. Manufacturing details of hip spacers

Study	In vivo/ in vitro ^a	Antibiotic (per 40 g PMMA)	Infecting organism ^b	Design ^c	Metallic components ^d
Abendschein (1992)	v	tobramycin	n.r.	m	none
Affatato et al. (2003)	t	gentamicin	n.r.	s	cylindrical rod of SS
Anagnostakos et al. (2005)	t	gentamicin, vancomycin teicoplanin, synercid (various concentrations)	SA, SE MRSA, <i>E. faecalis</i>	s	none
Barrack (2002)	v	3.6 g tobramycin 1 g vancomycin	n.r.	m	1 Rush pin
Bertazzoni Minelli et al. (2004)	t	gentamicin, vancomycin	n.r.	s	hollow cylindrical rod
Desmukh et al. (1998)	v	unknown	n.r.	m	Küntcher nail
Duncan et al. (1993)	v	2.4 g tobramycin 1 g vancomycin penicillin G	SA, SE, <i>E. coli</i> , <i>Streptococcus</i>	s	SS endoskeleton
Durbhakula et al. (2004)	v	2.4 g tobramycin 1 g vancomycin	SA, SE, <i>Proteus</i> , MRSA, <i>Enterobacter</i> , <i>E. coli</i>	s	1 Rush pin
Greene et al. (1998)	t	4 g tobramycin 4 g vancomycin	SA <i>B. subtilis</i>	s	none
Haddad et al. (1999)	v	2.4–3.6 g tobramycin 1–1.5 g vancomycin	n.r.	s	SS endoskeleton
Holtom et al. (1998)	t	4 g vancomycin	<i>B. subtilis</i>	s	none
Hsieh et al. (2004)	v	vancomycin, gentamicin, teicoplanin, aztreonam, piperacillin	mostly staph. species	s	>2 K-wires
Isiklar et al. (1999)	v	2–3 g vancomycin	SE, MRSE	m	2–3 Steinmann pins
Ivarsson et al. (1994)	v	gentamicin	<i>Enterococcus</i> , <i>Klebsiella</i> , CNS, <i>Propionibacteria</i> , <i>Streptococcus B</i>	m	none
Jahoda et al. (2003)	v	gentamicin	n.r.	m	1 K-wire
Kelm et al. (2001)	v	n.r.	n.r.	s	none
Koo et al. (2001)	v	1 g gentamicin 1 g vancomycin 1 g cefotaxime	SA, SE <i>Enterobacter cloacae</i> <i>P. aeruginosa</i>	s	none
Kraay et al. (1992)	v	2 g tobramycin	1 × SE (rest: unknown)	m	cerclage wire
Leunig et al. (1998)	v	gentamicin	SA, CNS	m	plates, screws
Magnan et al. (2001)	v	0.95 g gentamicin 1 g vancomycin	SA, SE, <i>P. aeruginosa</i> <i>E. coli</i> , <i>M. tuberculosis</i> , β -hem. <i>streptococcus</i> , n.r.	s	hollow cylindrical rod of SS
Masri et al. (1998)	v	1.2–4.8 g tobramycin 1–2 g vancomycin	n.r.	s	SS endoskeleton
McGrory et al. (2002)	v	1.5 g vancomycin	MRSA	m	endoprosthetic head
Morimoto et al. (2003)	v	40 mg gentamicin 6 g vancomycin	MRSA	m	gamma locking nail
Pearle et al. (2002)	v	tobramycin	n.r.	s	2 Steinmann pins
Ries et al. (1999)	v	1.2–3.6 g tobramycin 1 g vancomycin	n.r.	s	intramed. nail/pins
Schöllner et al. (2003)	t	0.5 g gentamicin	n.r.	s	2 K-wires
Shin et al. (2002)	v	n.r.	n.r.	s	femoral endoprosthesis
Takahira et al. (2003)	v	1.5 g gentamicin 2 g vancomycin	SA, SE, MRSA, <i>E. coli</i>	m	Ender nail/K-wires with cerclage wires
Yamamoto et al. (2003)	v	0.5 g gentamicin 0.5 g gentamicin + 1 g vancomycin	4 × CNS, 4 × SE, 3 × MRSA, 1 × <i>E. coli</i> , 1 × <i>P. aeruginosa</i>	m/s	2 K-wires
Younger et al. (1997)	v	tobramycin, penicillin G, vancomycin, ceftizoxime streptomycin	24 × SE 7 × SA, <i>streptococci</i> , others	s	SS endoskeleton
Wentworth et al. (2002)	v	3.6 g tobramycin 1.5 g vancomycin	34 × SA, 30 × SE 11 × <i>Enterococcus</i> , etc.	s	SS endoskeleton
Zilkens et al. (1990)	v	gentamicin	SA, <i>P. mirabilis</i>	m/s	metallic telescopic shaft

Footnotes Table 1:

^a v – in vivo, t – in vitro^b CNS – Coagulase negative staphylococci, MR – methicillin-resistant, SA – *Staphylococcus aureus*, SE – *Staphylococcus epidermidis*^c m – manually shaped, s – standardized formed, n.r. – not reported.^d K – Kirschner, SS – stainless steel

et al. 2005). However, these values may be false-negative if the patient has already been treated with antibiotics. Radiological findings depend on the stage of the infection, and may be normal. A preoperative hip aspiration has been performed routinely by some authors (Isiklar et al. 1999, Takahira et al. 2003), whereas others have found it to be of minor value, since the reported rates of negative preoperative aspiration are in the 7–50% range (Koo et al. 2001). Also, intraoperative findings may suggest an infection despite a negative preoperative aspiration (Kraay et al. 1992). Multiple biopsy samples from the infected area should help to clarify and distinguish a contamination from an infection of any clinical significance.

Pathogenic organisms

Most of the reported infections were caused by *Staphylococcus aureus*, *Staphylococcus epidermidis*, methicillin-resistant *Staphylococcus aureus*, and *Eschericia coli* (Table 1). In a few cases, a polymicrobial infection has been diagnosed. Depending on the profile of the infecting organism, the local therapy has been complemented with a wide range of oral and/or parenteral antibiotics, amongst which cephalosporins have been administered most frequently (Table 2).

Clinical experience

In one of the latest reports by the PROSTALAC team, Haddad et al. (1999) described healing of the infection in 77 of 81 hips. The mean Harris hip score increased from 34 points before spacer implantation to 56 during stages and 76 at the time of reimplantation. In a study prior to that, the great majority of patients (43/48) were reportedly satisfied with the outcome of the treatment (Younger et al. 1997). Such subjective reports have been supported by the study of Koo et al. (2001) who used the Merle d'Aubigne hip score and found an increase from 5.9 to 14.6 points. Takahira et al. (2003) reported a similar improvement after spacer

implantation using the hip score of the Japanese Orthopaedic Association (an increase from 30 to 73 points).

Only one study has appeared that has compared the two procedures of the two-stage protocol (Girdlestone and spacer implantation) (Hsieh et al. 2004). It could be shown that the spacer implantation had a significantly lower complication rate. Between stages, the patients achieved a higher hip score rate, and at re-implantation there was a shorter operative time, less loss of blood, and a lower transfusion requirement, indicating that the spacer is probably the superior technique in the treatment of late hip joint infections.

Furthermore, the treatment of infection by using a spacer seems to offer great advantages, even in cases with massive bone loss of the proximal femur or the acetabulum (Duncan et al. 1993, Younger et al. 1998, Isiklar et al. 1999, Hsieh et al. 2005). The prosthesis re-implantation can be a technically demanding procedure due to leg length discrepancy, soft-tissue shortening and disuse osteoporosis. The implantation of a spacer in such cases gives the patient a functional joint during the interim period. Duncan et al. (1993) and Hsieh et al. (2005) reported encouraging results in the treatment of hip infections by spacer implantation followed by reconstruction with allografts. None of the patients had any recurrence of infection, and the joint function was enhanced between stages.

In addition to the material properties of the spacers, an optimal interaction and articulation between the bone and the spacer favors a positive result of the joint replacement. The insertion of a standardized, articulating and antibiotic-impregnated prosthesis into the bone reduces the risk of crepitus during hip mobilization and helps to preserve the bone stock (Ries and Jergesen 1999, Shin et al. 2002). This method has been reported to increase hip mobility and reduce pain during stages and after re-implantation (Duncan and Beauchamp 1993, Younger

Table 2. Clinical response, complications and follow-up

Study	Hips	Antibiotics p.o./i.v.	Complication	Weeks between stages	Follow-up (months)
Abendschein (1992)	1	n.r.	none	34	24
Barrack (2002)	12	n.r.	none	6–12	24–48
Desmukh et al. (1998)	5	n.r.	none	n.r.	n.r.
Duncan et al. (1993)	15	n.r.	3 × dislocation 1 × sciatic paresis (resolved) 1 × peroneal paresis (resolved)	4–40	25–54
Durbhakula et al. (2004)	20	n.r.	2 × fractures 2 × dislocations	10–21	26–67
Haddad et al. (1999)	81	n.r.	n.r.	n.r.	24–114
Hsieh et al. (2004)	58	n.r.	2 × infection persistence 1 × infection recurrence 2 × dislocations 2 × fractures	7–40	24–96
Isiklar et al. (1999)	10	rifampicin vancomycin ceftazidime	1 × spacer dislocation 1 × femur fracture	3–14	16–36
Ivarsson et al. (1994)	5	cephalosporin clindamycin cloxacillin	1 × spacer dislocation 1 × subtrochanteric fracture	3–8	9–24
Jahoda et al. (2003)	29	n.r.	1 × infection persistence 2 × fractures 5 × dislocations	6–28	n.r.
Kelm et al. (2001)	7	n.r.	none	n.r.	8
Koo et al. (2001)	22	vancomycin, cefotaxime ciprofloxacin, cefamandole	2 × femur fracture (intraop.) 2 × peroneal paresis 3 × heterotopic ossification	6–12	24–78
Kraay et al. (1992) (average)	7	n.r.	none	n.r.	15
Leunig et al. (1998)	12	n.r.	5 × dislocation 1 × protrusion 1 × fracture	8–30	27
Magnan et al. (2001)	10	teicoplanin, ciprofloxacin	2 × acetabular bone graft 1 × dislocation	13–39	24–48
Masri et al. (1998)	49	n.r.	n.r.	6–46	n.r.
McGrory et al. (2002)	1	naftillin, rifampicin	none	n.r.	12
Morimoto et al. (2003)	1	n.r.	none	6	30
Pearle et al. (2002)	n.r.	tobramycin	n.r.	n.r.	n.r.
Ries et al. (1999)	n.r.	n.r.	n.r.	n.r.	n.r.
Shin et al. (2002)	8	n.r.	none	n.r.	n.r.
Takahira et al. (2003)	9	n.r.	1 × reinfection	6–19	10–55
Yamamoto et al. (2003)	17	n.r.	1 × fracture 1 × dislocation	13–40	14–62
Younger et al. (1997)	61	vancomycin cefamandole	1 × periprosthetic fracture 5 × dislocation 4 × reinfection	5–42	24–63
Wentworth et al. (2002)	135	n.r.	15 × dislocation 12 × infection		
Zilkens et al. (1990)	1	wide-spectrum penicillin	none	26	43
n.r.: not reported.					

et al. 1997, Koo et al. 2001, Magnan et al. 2001, Takahira et al. 2003).

Most spacer patients were mobile during stages, either on crutches with toe touch and/or partial

weight bearing. Leunig et al. (1998) reported dislocations of the hip in 5 of 12 patients, Magnan et al. (2001) reported a dislocation rate of 1/10, and Duncan et al. (1993) reported dislocations in 3 of

13 patients. Ries and Jergesen (1999), Koo et al. (2001), Shin et al. (2002) and Takahira et al. (2003) did not observe any dislocation during implantation of the spacer (Table 2).

The period between stages varied. Based on laboratory data and the progress of each infection, the re-implantation was carried out after a mean period of 3–4 months. Usually, no difficulties were reported at the time of spacer removal. Re-infections—either with the primary organism or with another bacterium—were rare and were only found in two studies (Table 2). A prolonged implantation period might actually endanger the outcome of the treatment since subtherapeutic levels of antibiotic(s) might be eluted from the spacer, and the antibiotic-impregnated cement itself provides an excellent environment for the development of resistant bacterial strains (Duncan and Masri 1994, Thomes et al. 2002).

On the whole, the overall success rates of the hip replacements were reported to be 80–98% (data not shown).

Antibiotic elution

Masri et al. (1994) measured intraarticular antibiotic concentrations in the first days after the insertion of vancomycin/tobramycin-loaded spacers. They confirmed the in-vitro results reported by Greene et al. (1998) and showed that tobramycin eluted better than vancomycin. Peak concentrations on day 1 were 107 µg/mL for tobramycin and 19 µg/mL for vancomycin, determined from the wound drainage fluids. These concentrations were 10–30 fold higher than the MICs of the infecting organisms. An increase in the tobramycin dose enhanced the elution of tobramycin and vancomycin, whereas an increase in the vancomycin concentration lacked such an effect (Masri et al. 1998). A sufficient degree of elution of antibiotics from PROSTALAC could be measured over a period of at least 4 months (Masri et al. 1998). The duration of the spacer implantation did not have a significant effect on the elution characteristics of either antibiotic.

Isiklar et al. (1999) reported mean concentrations of 57 µg/mL vancomycin on day 1 from vancomycin-impregnated spacers in the treatment of orthopedic implant-related *Staphylococcus epidermidis* infections, also determined from the drainage fluid.

A recent in-vitro study has investigated the efficacy of single antibiotic- and biantibiotic-loaded spacers with regard to bacterial growth inhibition and antibiotic release (Anagnostakos et al. 2005). Gentamicin/vancomycin-loaded spacers were the most effective in growth inhibition of *S. epidermidis* and MRSA, whereas gentamicin/teicoplanin-impregnated spacers showed the best results against *E. faecalis* and *S. aureus*.

Reports on the elution characteristics of spacers are encouraging, but require further investigations about the exact nature of the release mechanism in vivo. In-vivo (Masri et al. 1998) and in-vitro studies (Anagnostakos et al. 2005) have shown a sufficient degree of antibiotic elution; however, both of these studies have limitations. In the first study, no data were reported on the antimicrobial properties at specific antibiotic concentrations, and in the latter one, the experimental conditions were different from normal conditions in vivo. An in-vivo animal model might perhaps solve this question.

Some concerns have been expressed regarding the ideal re-implantation time, and whether spacer removal that is too early or too late with prosthesis re-implantation might be associated with persistence or recurrence of infection. Bertazzoni Minelli et al. (2004) studied antibiotic elution from explanted spacers. 0.05–0.4% gentamicin and 0.8–3.3% vancomycin (of the initial amounts present) were released in vitro over a time period of 10 days, indicating that a sufficient degree of antibiotic release can persist over several months.

Following surgery, the outcome of infections can be particularly dramatic because of the extent of soft tissue, and therefore systemic antibiotic therapy should be given. Unfortunately, such supporting antibiotic treatments are not without risks—as reported by Koo et al. (2001). In that study, the authors described the occurrence of a transient liver dysfunction and bone marrow depression following the simultaneous implantation of an antibiotic-loaded spacer and intravenous treatment with antibiotics.

Holtom et al. (1998) found a positive correlation between the surface area of the vancomycin-loaded spacers and their elution characteristics in vitro. By increasing the surface-to-volume ratio from 0.24 (control-spacer) to 0.30, a 40% enhancement in

antibiotic release could be achieved. Greene et al. (1998) showed that tobramycin showed a higher release rate than vancomycin, and that Palacos allowed higher antibiotic elution than Simplex.

Mechanical stability

The mechanical stability of spacers is determined and influenced by many parameters, including geometry, ageing, storage, type of cement, the type and content of antibiotic(s), the presence of an endoskeleton, and standardization of its preparation (such as atmospheric composition during mixing and the frequency and duration of the particular mixing process) (Murray 1984, Leunig et al. 1998). Mechanical stress experiments with gentamicin-loaded spacers showed an average failure load of 1.6 kN (Schöllner et al. 2003). The inclusion of K-wires into the spacers prevented any dislocation of the fragments, but did not improve the mechanical properties significantly. In contrast to that, Kelm et al. (2001) reported an average failure load of 20 kN with antibiotic-loaded cement, not including any supporting metal components. Recently, Affatato et al. (2003) investigated in an in-vitro model for the changes in PMMA polymer conformation induced by wear. Although the wear behavior varied with the area of the spacer and the amount of debris was higher than in tests with no temporary prostheses, the authors concluded that partial weight bearing can be allowed, since at the time of prosthesis re-implantation any particle debris can be removed by jet lavage.

The mechanical strength of cement is not only influenced by the type of antibiotic and atmospheric pressure, but also by the ratio in which the antibiotics are mixed into the cement (Lautenschlager et al. 1976). Proportional weights of up to roughly 5% have a negligible influence on the mechanical strength of the resulting cement (Levin 1975, Lautenschlager et al. 1976, Murray 1984), whereas larger amounts of antibiotic powder will make the cement harder to mix and increase the possibility of lack of homogeneity. There is no quantitative information available regarding the ideal antibiotic/cement ratio, but most surgeons do not exceed a ratio of 10%. However, Hsieh et al. (2005) recently reported an antibiotic mixture ratio of up to 20% and had no difficulty in fabricating the prosthesis.

In addition to the manufacturing process, other factors might compromise the function of the spacer, including the residual bone quality after the first surgery, or deficient soft tissue. Although numerous initial strength tests for antibiotic-impregnated cement blocks or discs have been carried out (Lautenschlager et al. 1976, Lidgren et al. 1987, Askew et al. 1990, Armstrong et al. 2002, Lewis 2003), only the studies by Kelm et al. (2001) and Schöllner et al. (2003) attempted to provide hard static data on these constructs. Unfortunately, the clinical relevance of these reports is hampered by the limited number of spacers investigated and the experimental conditions (an axial strength test does not represent the stress that a spacer is being exposed to in the human body). The mechanical strength of the spacers could be increased by the addition of a metallic endoskeleton, although the benefits of such a construct have not been thoroughly determined. Also, a spacer fracture exposing the metal may lead to bacterial recolonization and/or re-infection. In addition, studies should be conducted to investigate the antibiotic elution profile of spacers with metal, in order to detect any possible alteration in the release characteristics.

New techniques

The increase in the popularity of spacers during the treatment of hip joint infections in the past years has fostered the search for new techniques for quick and simple intraoperative manufacture. Ries and Jergesen (1999) and Shin et al. (2002) recommended the use of a rubber bulb portion of an irrigation syringe as a mold to shape the proximal end of the spacer, while Barrack (2002) manufactured different spacers by using rod pins of various lengths and diameters. Such an approach would enable the surgeon to build up a stock of premanufactured spacers, from which the appropriate shape could be selected during surgery. Ries and Jergesen (1999), Barrack (2002) and Shin et al. (2002) reported using such spacers for successful eradication of infection—and preservation of articulation between the spacer and the acetabulum in conjunction with satisfying mechanical strength of the prosthesis.

Conclusion

A choice between one-stage and two-stage proce-

dures must be made in the treatment of an infection of the hip joint. Should the patient undergo a two-stage protocol, the implantation of antibiotic-loaded spacers is currently the most commonly used method. Here, we have reviewed the current data available and our conclusions can be summarized as follows:

- Standardized spacers appear to be superior to hand-made spacers
- The combination of two antibiotics is advisable, due to the enhanced elution of both agents and the wider antimicrobial spectrum
- For an aminoglycoside-glycopeptide combination, the glycopeptide should be included at a higher dose due to its inferior release characteristics
- The total (additive) dose of the two antibiotics should not exceed 10% of the weight of the cement, in order to maintain the mechanical strength of the spacer
- Insertion of metallic components into the cement during the spacer's manufacturing process may increase its stability, but the release of antibiotics after metal insertion has not been evaluated
- A complementary, systemic antibiotic treatment during the first weeks between stages is necessary to prevent an infection due to hematogenous spread, but it should be noted that the selected antibiotics ought to differ from the spacer's antibiotics.

Better data on all of these issues are clearly desirable. The ideal ratio of antibiotic and cement for hip spacers is still unknown and requires quantification. In addition, in future studies more attention should be paid to possible improvements in the mixing process, which may result in a more homogeneous antibiotic/cement mixture. We would also welcome further investigations into the enhanced strength of spacers by inclusion of metal endoskeleton at different antibiotic concentrations. It should, however, be noted that despite the importance of in vitro studies for all these parameters, clinical trials are imperative to confirm and substantiate the results.

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- Abendschein W. Salvage of infected total hip replacement: use of antibiotic/ PMMA-Spacer. *Orthopedics* 1992; 15 (2): 228-9.
- Affatato S, Mattarozi A, Taddei P, Robotti P, Soffiatti R, Sudanese A, Toni A. Investigations on the wear behaviour of the temporary PMMA-based hip Spacer-G. *Proc Inst Mech Eng (H)* 2003; 217 (1): 1-8.
- Anagnostakos K, Kelm J, Regitz T, Schmitt E, Jung W. In vitro evaluation of antibiotic release from and bacteria growth inhibition by antibiotic-loaded acrylic bone cement spacers. *J Biomed Mater Res B Appl Biomater* 2005; 72 (2): 373-8.
- Armstrong M S, Spencer R F, Cunningham J L, Gheduzzi S, Miles A W, Learmonth I D. Mechanical characteristics of antibiotic-laden bone cement. *Acta Orthop Scand* 2002; 73 (6): 688-90.
- Askew M J, Kufel M F, Fleissner P R, Gradisar I A, Salstrom S-J, Tan J S. Effect of vacuum mixing on the mechanical properties of antibiotic-impregnated polymethylmethacrylate bone cement. *J Biomed Mater Res* 1990; 24 (5): 573-80.
- Barrack R L. Rush pin technique for temporary antibiotic-impregnated cement prosthesis for infected total hip arthroplasty. *J Arthroplasty* 2002; 17 (5): 600-3.
- Bertazzoni Minelli E, Benini A, Magnan B, Bartolozzi P. Release of gentamicin and vancomycin from temporary human hip spacers in two-stage revision of infected arthroplasty. *J Antimicrob Chemother* 2004; 53 (2): 329-34.
- Buchholz H W, Engelbrecht E. Über die Depotwirkung einiger Antibiotika bei Vermischung mit dem Kunstharz Palacos. *Chirurg* 1970; 41: 511-5.
- Cercenado E, Garcia Leoni M E, Diaz M D, Sanchez-Carrillo C, Catalan P, De Quiros J C, Bouza E. Emergence of teicoplanin-resistant coagulase-negative staphylococci. *J Clin Microbiol* 1996; 34 (7): 1765-8.
- Deshmukh R G, Thevarajan K, Kok C S, Sivapathasundaram N, George S V N. An intramedullary cement spacer in total hip arthroplasty. *J Arthroplasty* 1998; 13 (2): 197-9.
- Duncan C P, Beauchamp C. A temporary antibiotic-loaded joint replacement system for management of complex infections involving the hip. *Orthop Clin North Am* 1993; 24 (4): 751-9.
- Duncan C P, Masri B A. The role of antibiotic-loaded cement in the treatment of an infection after a hip replacement. *J Bone Joint Surg (Am)* 1994; 76 (11): 1742-51.
- Durbhakula S M, Czajka J, Fuchs M D, Uhl R L. Spacer endoprosthesis for the treatment of infected total hip arthroplasty. *J Arthroplasty* 2004; 19 (6): 760-7.
- Ger E, Dall D, Miles T, Forder A. Bone cement and antibiotics. *S Afr Med J* 1977; 51 (9): 276-9.
- Greene N, Holtom P D, Warren C A, Ressler R L, Shepherd L, McPherson E J, Patzakis M J. In vitro elution of tobramycin and vancomycin polymethylmethacrylate beads and spacers from Palacos and Simplex. *Am J Orthop* 1998; 27 (3): 201-5.
- Haaker R, Senge A, Kramer J, Rubenthaler F. Osteomyelitis after endoprostheses. *Orthopäde* 2004; 33: 431-8.

- Haddad F S, Masri B A, Garbuz D S, Duncan C P. The treatment of the infected hip replacement: the complex case. *Clin Orthop* 1999; (369): 144-56.
- Holtom P D, Warren C A, Greene N W, Bravos P D, Ressler R L, Shepherd L, McPherson E J, Patzakis M J. Relation of surface area to in vitro elution characteristics of vancomycin-impregnated polymethylmethacrylate spacers. *Am J Orthop* 1998; 27 (3): 207-10.
- Hsieh P-H, Shih C-H, Chang Y-H, Lee MS, Shih H-N, Yang W-E. Two-stage revision hip arthroplasty for infection: comparison between the interim use of antibiotic-loaded cement beads and a spacer prosthesis. *J Bone Joint Surg (Am)* 2004; 86 (9): 1989-97.
- Hsieh P-H, Shih C-H, Chang Y-H, Lee MS, Yanh W-E, Shih H-N. Treatment of deep infection of the hip associated with massive bone loss. Two-stage revision with an antibiotic-loaded interim cement prosthesis followed by reconstruction with allograft. *J Bone Joint Surg (Br)* 2005; 87 (6): 770-5.
- Isiklar Z U, Demirörs H, Akpinar S, Tandogan R N, Alparslan M. Two-stage treatment of chronic staphylococcal implant-related infections using Vancomycin-impregnated PMMA-Spacer and rifampicin containing antibiotic protocol. *Bull Hosp Jt Dis* 1999; 58 (2): 79-85.
- Ivarsson I, Wahlström O, Djerf K, Jacobsson S-A. Revision of infected hip replacement. Two-stage procedure with a temporary gentamicin spacer. *Acta Orthop Scand* 1994; 65 (1): 7-8.
- Jahoda D, Sosna A, Landor I, Vavrik P, Pokorný D. Canalized spacer in the treatment of deep infection of total hip arthroplasty using a two-stage reimplantation. *Oper Orthop Traumatol* 2003; 1: 57-69.
- Joseph T N, Chen A L, Di Cesare P E. Use of antibiotic-impregnated cement in total joint arthroplasty. *J Am Acad of Orthop Surg* 2003; 11 (1): 38-47.
- Kelm J, Regitz T, Schmitt E. Infektsanierung durch resistenzgerechte Hüftinterimsprothese und Antibiotikakette. *J DGPW* 2001; 23: 61-2.
- Koo K-H, Yang J-W, Cho S-H, Song H-R, Park H-B, Ha Y-C, Chang J-D, Kim S-Y, Kim Y-H. Impregnation of vancomycin, gentamicin and cefotaxime in a cement spacer for two-stage cementless reconstruction in infected total hip arthroplasty. *J Arthroplasty* 2001; 16 (7): 882-92.
- Kraay M J, Goldberg V M, Figgie H E III. Use of an antibiotic impregnated polymethyl methacrylate intramedullary spacer for complicated revision total hip arthroplasty. *J Arthroplasty (Suppl)* 1992; 7: 397-402.
- Krcmery V, Trupl J, Dragona L, Lacka J, Kukuckova E, Oravcova E. Nosocomial bacteremia due to vancomycin-resistant *Staphylococcus epidermidis* in four patients with cancer, neutropenia, and previous treatment with vancomycin. *Eur J Clin Microbiol Infect Dis* 1996; 15 (3): 259-61.
- Lautenschlager E P, Jacobs J J, Marshall G W, Meyer P R Jr. Mechanical properties of bone cements containing large doses of antibiotic powders. *J Biomedical Mater Res* 1976; 10 (6): 929-38.
- Leunig M, Chosa E, Speck M, Ganz R. A cement spacer for two-stage revision of infected implants of the hip-joint. *Int Orthop* 1998; 22 (4): 209-14.
- Levin P D. The effectiveness of various antibiotics in methacrylate. *J Bone Joint Surg (Br)* 1975; 57 (2): 234-7.
- Lewis G. Fatigue testing and performance of acrylic bone-cement materials: State-of-the-art review. *J Biomed Mater Res* 2003; 66 (1): 457-86.
- Lidgren L, Bodelind B, Moller J. Bone cement improved by vacuum mixing and chilling. *Acta Orthop Scand* 1987; 58 (1): 27-32.
- Magnan B, Regis D, Biscaglia R, Bartolozzi P. Preformed acrylic bone cement spacer loaded with antibiotics. Use of two-stage procedure in 10 patients because of infected hips after total replacement. *Acta Orthop Scand* 2001; 72 (6): 591-4.
- Masri B A, Duncan C P, Beauchamp C P, Paris N J, Arntorp J. Tobramycin and Vancomycin elution from bone cement. An in vivo and in vitro study. *Orthop Trans* 1994; 18:130.
- Masri B A, Duncan C P, Beauchamp C P. Long-term elution of antibiotics from bone-cement. *J Arthroplasty* 1998; 13 (3): 331-8.
- McGrory B J, Shinnick J, Ruterbories J. A simple method of intra-articular antibiotic delivery in infected hip arthroplasty. *Am J Orthop* 2002; 31 (5): 250-1.
- Morimoto S, Futani H, Ogura H, Okayama A, Maruo S. Successful reimplantation of total femoral prosthesis after deep infection. *J Arthroplasty* 2003; 18 (2): 216-20.
- Murray W R. Use of antibiotic-containing bone cement. *Clin Orthop* 1984; (190): 89-95.
- Neu H C. The crisis in antibiotic resistance. *Science* 1992; 257 (5073): 1064-72.
- Pearle A D, Sculco T P. Technique for fabrication of an antibiotic-loaded cement hemiarthroplasty (ANTILOCH) prosthesis for infected total hip arthroplasty. *Am J Orthop* 2002; 31 (7): 425-7.
- Ries M D, Jergesen H. An inexpensive molding method for antibiotic-impregnated cement spacers in infected total hip arthroplasty. *J Arthroplasty* 1999; 14 (6): 764-5.
- Schöllner C, Fürderer S, Rompe J-D, Eckardt A. Individual bone cement spacers (IBCS) for septic hip revision – preliminary report. *Arch Orthop Traum Surg* 2003; 123 (5): 254-9.
- Shin S S, Della Valle C J, Ong B C, Meere P A. A simple method for construction of an articulating antibiotic-loaded cement spacer. *J Arthroplasty* 2002; 17 (6): 785-7.
- Takahira N, Itoman M, Higashi K, Utsiyama K, Miyabe M, Naruse K. Treatment outcome of two-stage revision total hip arthroplasty for infected hip arthroplasty using antibiotic-impregnated cement spacer. *J Orthopedic Sci* 2003; 8 (1): 26-31.
- Thomes B, Murray P, Bouchier-Hayes D. Development of resistant strains of *Staphylococcus epidermidis* on gentamicin-loaded bone cement in vivo. *J Bone Joint Surg (Br)* 2002; 84 (5): 758-60.
- Ure K J, Amstutz H C, Nasser S, Schmalzried T P. Direct-exchange for the arthroplasty treatment of infection after total hip arthroplasty. *J Bone Joint Surg (Am)* 1998; 80 (7): 961-8.

- Wagner H, Wagner M. Infizierte Hüftgelenksprothesen. Gesichtspunkte für den einzeitigen und zweizeitigen Prothesenwechsel. *Orthopäde* 1995; 24 (4): 314-8.
- Wahlig H. Über die Freisetzungskinetik von Antibiotika aus Knochenzementen – Ergebnisse vergleichender Untersuchungen in vitro und in vivo. *Aktuelle Probl Chir Orthop* 1987; 31: 221-6.
- Wendt C, Rüden H, Edmond M. Vancomycin-resistente Enterokokken. *Dtsch Ärzteblatt* 1998; 95: 1284-91.
- Yamamoto K, Miyagawa N, Masaoka T, Katori Y, Shishido T, Imakiire A. Clinical effectiveness of antibiotic-impregnated cement spacers for the treatment of infected implants of the hip joint. *J Orthop Sci* 2003; 8 (6): 823-8.
- Younger A S E, Duncan C P, Masri B A, McGraw R W. The outcome of two-stage arthroplasty using a custom-made interval spacer to treat the infected hip. *J Arthroplasty* 1997; 12 (6): 615-23.
- Younger A S, Duncan C P, Masri B A. Treatment of infection associated with segmental bone loss in the proximal part of the femur in two stages with use of an antibiotic-loaded interval prosthesis. *J Bone Joint Surg (Am)* 1998; 80 (1): 60-9.
- Zilkens K-W, Casser H-R, Ohnsorge J. Treatment of an old infection in a total hip replacement with an interim spacer prosthesis. *Arch Orthop Trauma Surg* 1990; 109 (2): 94-6.