Two-Stage Exchange Knee Arthroplasty: Static Spacers

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Two-stage exchange arthroplasty is currently the most commonly used treatment for infected total knee replacement in North America. Published reports have demonstrated a variable success rate for the procedure ranging from 67 to 91 % [1–5]. The procedure allows for placement of an antibiotic-cement spacer in the knee for local delivery of antibiotics, and at the same time provides a chance for systemic antibiotic therapy to effectively eradicate residual planktonic bacteria that remain in the knee after surgical debridement of the bacterial biofilm. Spacers also reduce dead space and maintain tension in the soft tissues to avoid contractures and potentially improve healing.

Cement and Antibiotic Elution

Elution of antibiotic from cement is a passive phenomenon in which antibiotics diffuse out of pores, cracks, and voids in the cement [6]. Elution rate and duration vary based on the type and dose of antibiotic used (first order kinetics) [7]. They also depend on the type and preparation of cement. Highly porous cement has been shown to have a higher and longer elution of antibiotics compared with its low porosity counterpart [8, 9]. A recent study [10] found that when antibiotic-impregnated polymethylmethacrylate (PMMA) products were mixed under atmospheric pressure, Palacos R+G (Zimmer, Warsaw, IN) produced a greater 5-day antimicrobial activity in vitro than Simplex P with tobramycin (Stryker, Kalamazoo, MI). This was attributed to the higher viscosity of Palacos [11, 12]. Further, vacuum-mixing increased their antimicrobial activity, with the highest increase seen with Palacos [10]. These findings corroborate the results of an earlier study showing higher antibiotic elution from vacuum-mixed Palacos [11]. The amount of antibiotics released from cement shows an exponential decline after day 1 of implantation [10, 11, 13]. Increasing the dose of the antibiotic leads to a higher and longer elution, not only due to the simple increase in concentration gradient for diffusion, but also by virtue of increased porosity of the cement [13]. In one study, low-dose antibiotics (1.0 g per 40 g of PMMA) resulted in an effective elution for an average of 2 days, intermediate-dose antibiotics (4 g per 40 g of PMMA) were effective for up to 21 days whereas high-dose antibiotics (8 g per 40 g of PMMA) had an elution that lasted for up to 60 days in vitro [14]. Therefore, hand-mixing of higher doses of antibiotics into the cement mixture is needed to treat prosthetic joint infections, whereas the low-dose antibiotics in commercial preparations are indicated for prophylaxis. They are currently FDA-approved for

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use in second-stage reimplantation when it is important to consider the mechanical strength of the cement-implant interface [10].

Antibiotic Types and Doses

Selection of antibiotics to be added to the cement spacer should be based on the type of the infecting organism. If the organism is unknown, antibiotics should be targeted against the most common pathogens causing prosthetic joint infection, namely methicillin-sensitive *Staphylococcus aureus*, coagulase-negative Staphylococci, *Staphylococcus* epidermidis, *Streptococcus*, *Enterococcus*, methicillin-resistant *S. aureus,* and Gram-negative bacteria [15–17]. Antibiotics used should also be heat stable, water soluble, and with a low allergenic potential [18]. The most commonly used antibiotics are vancomycin, tobramycin, gentamicin, and cephalosporins [18]. Vancomycin and tobramycin are commercially available in powder form and are therefore used most commonly. Gentamicin and tobramycin are also present in premixed commercial preparations. Fungal infections, although rare, require adding antifungal agents to the spacer, the type and dose of which remain yet to be determined. Recent studies have shown promising elution of voriconazole from cement in vitro [19, 20], whereas effectiveness of amphotericin B in cement is still questionable [21–23].

Doses of antibiotics should ideally be determined based on a resultant elution that will remain above the minimum inhibitory concentration (MIC) of most pathogens for the entire duration of spacer implantation. This aims at avoiding the development of drug resistance that may occur as a result of subinhibitory concentration of antibiotics and to minimize adherence of organisms to the surface of the spacer. For gentamicin, as low as 0.5 g per 60 g of cement has been shown to result in a local concentration that is above the MIC of most organisms for the first 48 h following surgery while maintaining a low serum concentration that avoids nephrotoxicity [24]. Adding 4 g of tobramycin or 4 g of vancomycin to 40 g of cement was reported to result in an in vitro elution that was above the MIC of *S. aureus* for 100 and 30 days respectively from Palacos, and for 20 and 15 days respectively from Simplex [13]. In cemented total hip arthroplasty using antibiotic-cement, measuring antibiotic concentration in hemovac fluid showed adequate elution of tobramycin over a 48-h period, and a less predictable elution of vancomycin. Tobramycin (1.2 g) or vancomycin (0.5 g) was hand-mixed with 40 g of cement [25]. In an in vivo study, Masri et al. [26] recommended that at least 3.6 g of tobramycin and 1 g of vancomycin should be added to each 40 g package of bone cement when antibiotic-loaded cement spacers are used to treat an infected total hip or knee arthroplasty. The authors noted that although it has been shown that adding higher doses of antibiotics resulted in higher and more sustained release in vitro [2, 14], increasing the dose of vancomycin from 1 to 2 g per package did not result in a significantly increased elution in their study [26]. However, increasing the tobramycin dose to 3.6 g per pack and using vancomycin in combination with tobramycin had a positive effect on vancomycin elution [26]. Another in vivo study demonstrated that using 4 g of vancomycin per 40 g of cement resulted in bioactive levels of the antibiotic at the time of second-stage surgery (average 107 days) [27]. Springer et al. showed that adding a total of 10.5 g of vancomycin and 12.5 g of gentamicin to a cement spacer made from Simplex bone cement did not result in systemic toxicity in a group of 34 patients with infected total knee arthroplasty. One patient had a temporary elevation in serum creatinine [17]. Despite these findings, systemic side effects of antibiotic-containing spacers have been reported in the literature [28, 29]. Spacers containing 2.9 g of gentamicin [28] and 3.6 g of tobramycin [29] resulted in acute renal failure in two elderly patients with mild preexisting renal impairment in two separate case reports. In both cases, serum antibiotic concentration measured 2 μg/mL [28, 29]. Two cases of tobramycin-induced acute renal failure have also been reported [30].

Surgical Technique

After thorough debridement and removal of components with special attention to minimizing bone loss, a cement mold of the extension gap is fashioned. Three to four packs of acrylic bone cement polymer is mixed with the antibiotic powder in a bowl followed by application of the liquid monomer. The mix is stirred with a spatula. The cement is allowed to cure until it is firm and is then placed in the extension gap while the knee is distracted. The cement block should be large enough to maintain adequate tension in the soft tissues and wide enough to rest on the cortical rim of the tibia [31]. The cement is allowed to harden with the knee in the extended position. Different techniques have been described to enhance fixation of the spacer block to the femur and tibia and to prevent migration. Superior and inferior pegs could be fashioned to fit into the femur and tibia, respectively [32]. Adding longer intramedullary extensions of the spacer has been described [31], with the advantage of antibiotic delivery into the medullary canal. Another technique with potential benefit in infected knees with deficient bone and collateral ligaments involves the use of an intramedullary nail inserted into the distal femur and proximal tibia. Cement is then introduced into the metaphyses, around the nail, and underneath the patella providing a state of "temporary knee fusion." This helps to achieve soft tissue healing, especially if a muscle flap is used in patients with chronically infected knees [33]. The surgeon must weigh the risk of using a metallic implant in the setting of chronic infection against the benefit of additional stability provided by the nail.

Indications for Static Spacers

Spacers were designed to facilitate reimplantation by minimizing soft tissue scarring and bone loss. In the 1980s, two-stage reimplantation was often done with no interim antibiotic spacer placed. In the 1990s, use of static cement spacers in the interim period became widespread [34]. Articulating spacers have been increasingly used since the late 1990s with the goal of improving quality of life in the period between stages as more knee flexion is permitted. Commercial molds, metal molds, implants, and hand-made spacers are used to create articulating spacers. They are designed to facilitate reimplantation by minimizing bone loss and soft tissue contracture and facilitating exposure. Another potential advantage is better ultimate knee flexion range following the second stage due to decreased immobilization between stages. However, an articulating spacer would not be the ideal choice in chronically infected knees with significant bone loss, extensor mechanism disruption, and collateral ligament insufficiency. It should also be avoided in patients with history of poor compliance and dementia [16]. In such cases, more stability is usually advantageous to allow healing, especially when plastic flaps are used. Joint immobilization has the added benefit of minimizing complications such as wound dehiscence, knee dislocation, fractures, spacer fracture, and particulate debris generation caused by the cement-on-cement articulation in a dynamic spacer [33, 35–37]. Complications related to static spacers are generally caused by displacement of an undersized static spacer block, which may result in significant bone loss, capsular contracture, and quadriceps scarring [31]. External bracing is also necessary with the use of static spacers.

Outcomes

Prospective randomized studies comparing the two spacer types are currently lacking. The vast majority of the studies citing improved range of motion [38], patient satisfaction [37], and ease of exposure at the time of reimplantation [39] with the articulating spacer report on individual case series with or without historical controls. Haddad et al. reported a 91 % success rate with the use of the PROSTALAC knee spacer in a group of 45 patients with infected knee arthroplasty. They noted decrease incidence of tibiofemoral dislocation in the group of patients that received a more constrained version of the PROSTALAC [35].

Another study showed a 12 % reinfection rate with the use of an all-cement articulating spacer. A femoral component fracture occurred in one case [40]. On the other hand, Haleem et al. reported a 16 % reoperation rate of two-stage knee arthroplasty revision using a static cement spacer. Nine knees (9 %) had component removal for reinfection and six knees (6 %) were revised for aseptic loosening [1]. One study showed an overall success rate of 74.5 % in treatment of infected total knee with a two-stage protocol using a static antibiotic spacer, with reinfection with same or different organism as the end-point [2]. Retrospective studies comparing the two spacer types showed a trend towards better function with articulating spacers but with no significant difference noted. Freeman et al. [34] found no statistically significant difference in reinfection rates or in postoperative total Knee Society scores between knees treated with static and articulating spacers. Knee Society functional scores showed a trend toward being better in patients in the articulating spacer group, however those patients were also significantly younger than patients in the static spacer group [34]. Another retrospective study comparing dynamic and static spacers showed similar reinfection rates, Knee Society scores, and range of motion between the two spacer groups [16]. Four patients in the dynamic spacer group experienced complications related to tibiofemoral instability and femoral component fracture. Emerson et al. [38] showed that patients with dynamic spacers had better average range of motion at follow-up compared with patients who had static spacers (107.8° compared with 93.7°). No clinical outcome scores were used. The reinfection rate was the same between the two groups [38].

Summary

Antibiotic spacers are an important tool in the management of periprosthetic joint infection. The concept of spacers has evolved from a static block in which the knee is immobilized in full extension to more conforming articulating surfaces that allow more knee motion, in an attempt to improve patients' quality of life before and after reimplantation. Static spacers are still indicated in knees with significant bone and soft tissue compromise to avoid complications related to mobility in the absence of the proper amount of constraint. Increasing the amount of antibiotics added to the cement results in a higher and longer elution but could lead to potential systemic toxicity. It also reduces the mechanical strength of cement which becomes a concern if mobility and weight bearing are to be permitted. The ideal dose of antibiotics to be mixed with cement remains unclear. Large doses have been demonstrated to be clinically safe, but have not shown to be cost-effective in providing better infection control.

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