International Journal of Research in Orthopaedics
Ayekoloye CI et al. Int J Res Orthop. 2025 Mar;11(2):389-394
http://www.ijoro.org

DOI: https://dx.doi.org/10.18203/issn.2455-4510.IntJResOrthop20250462

Case Series

Static antibiotic loaded cement spacer application in 2-stage management of native and prosthetic hip joint infections: a case series and review of the literature

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Received: 08 October 2024
Revised: 19 November 2024
Accepted: 04 January 2025

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ABSTRACT

Two-stage revision including interval cement spacer application is the gold standard treatment for both prosthetic and native hip infection with joint destruction. We present a summarised case series of our experience of successfully treating 8 infected joints in 6 patients treated with 2-stage revision using interval static spacers. Two patients with 3 native joint infections and 4 patients with 5 prosthetic joint infections were treated with 2-stage arthroplasty with interval static spacer application consisting of static block spacers or cement beads. There were 2 females and 4 males. Mean age is 40.5 years and range 24-60 years. Mean interval between the first and second stage is 8weeks. One case has not undergone the second stage as he is unable to fund the operation. Organisms cultured include methicillin- sensitive staphylococcus aureus, enterococcus. All underwent cementless hip reconstruction with one patient undergoing hybrid hip reconstruction. At mean 36-month follow-up (range 30-44 months) all patients have normalized inflammatory markers and improvement in Oxford hip score (OHS) from pre-operative mean 16.6 (range 15-19) and post-operative mean OHS 43.7 (range 35-50). Patients continue to be followed up. We recommend this cement spacer option as part of a 2-stage procedure when faced with moderate to severe acetabular bone loss. It is effective in treating native or prosthetic hip joint infections and joint infections in patients with sickle cell haemoglobinopathy.

Keywords: Cement spacer, Haemoglobinopathy, Arthroplasty, Antibiotics

INTRODUCTION

Native hip joint infection with joint destruction as well as prosthetic hip joint infection can be best managed by 2-stage arthroplasty with thorough debridement and irrigation of the joint being the most important initial intervention.[1] This should then be followed by both high local and systemic antibiotic therapy to obtain complete eradication of infection before undertaking definitive second stage joint reconstruction. Success rate with this approach is above 90%.[1] Crucial to this 2-stage process is the implantation of antibiotic eluting cement spacer following the debridement. This can be self-fabricated or prefabricated, articulating, or non-articulating (static), monolithic (hemiarthroplasty) or separate femoral and acetabular articulating cement coated implant spacer components.[2] They can also be classified into self-fabricated, moulded, prefabricated, or cement coated implant spacers.[2] The choice of antibiotics is guided by the type and sensitivities of the infecting organism. In our environment, the use of over-the-counter antibiotics prior to presentation is not uncommon and can result in difficulty in isolating infective organisms when patients present with joint infection. Treatment of culture negative joint infections can be difficult as infecting organisms often cannot be identified and antibiotic sensitivities

cannot therefore be determined. A further problem is the presence of moderate to severe acetabular bone loss precluding the use of dynamic (articulating) cement spacer.

The objective of this study was to present a case series in summery form depicting our experience with the use of self-fabricated, non-articulating (static), high eluting multi-antibiotic cement spacer in the management of 8 infected native and prosthetic hip joints. Secondly, we review the types of cement spacer applications in 2-stage revision total hip replacement for infection.

CASE SERIES

Over a 5-year period from 2016 to 2021, 6 patients with 8 hip joint infections presented to our arthroplasty service. One patient presented with infected total hip arthroplasty; 3 patients presented with 4 infected hip hemiarthroplasties. Two of the patients had sickle cell disease with one presenting with bilateral infected hemiarthroplasties. The third patient underwent hemiarthroplasty for post-traumatic fracture neck of femur which subsequently became infected and had undergone multiple unsuccessful attempts at debridement and re-implantation at a peripheral hospital without eradicating the infection. The remaining 2 cases presented with infection of their native hip joints. One patient with sickle cell disease presented with infection of both hip joints that were already affected by sickle cell induced advanced femoral head osteonecrosis with secondary osteoarthritis. The other patient, a Jehovah's Witness developed hip infection by direct spread of infection from an infected intramedullary nail used to treat a post-traumatic fracture of the shaft of the femur. Details of patient demographics, microbiology, acetabular defect classification and functional results are shown in Table 1.

Table 1: Case series summary - table depicting patient demographics, pathology and outcome following 2-stage reconstruction for infection using self-fabricated static cement spacer.

Patient/ side	Age/ sex	Pathology	Diagnosis/prior surgery	Microbiology	Ace. class Paprosky	Pre/postop CRP	Pre/post -op OHS
1/Right	43 M	HbSS	Native hip joint sepsis	-ve culture	2B	42/<5	15/41
1/Left	43 M	HbSS	Native hip joint sepsis	-ve culture	2C	42/<5	15/?
2/Left	60 M	Trauma	Infected IM nail femur	-ve culture	2B	65/<5	17/48
3/Right	32 F	HbSS	Infected hip hemiarthroplasty	MSSA	3B	81/4.2	19/50
4/Right	24 M	HbSS	Infected hip hemiarthroplasty	-ve culture	2C	76.9/<5	15/38
4/Left	24 M	HbSS	Infected hip hemiarthroplasty	-ve culture	3A	76.9/<5	15/49
5/Left	52 F	Trauma	Infected hip hemiarthroplasty	Coag –ve *Staph aureus*	2A	32/5.3	18/45
6/Left	32 M	AVN	Infected THA	*Enterococcus*	3A	45/<5	19/35

Ace. class Paprosky=Paprosky acetabular bone defect classification[3]; pre-op OHS=pre-operative Oxford hip score; post-op OHS=post-operative Oxford hip score[4]; HbSS=sickle cell haemoglobinopathy; AVN=avascular necrosis; MSSA=methicillin sensitive *Staphylococcus aureus*; Coag -ve=coagulase negative

All patients presented with worsening hip pain, painful hip movements high inflammatory markers and positive ubiquitin scans. The patient with infected total hip arthroplasty presented in addition with discharging sinuses. All patients presenting with native hip joint sepsis presented with necrotic femoral heads. We proceeded directly to arthrotomy, excision of the femoral head and first stage debridement. For those presenting with infected hip hemiarthroplasties, there was evidence of significant acetabular erosion in all cases (Figure 1). We elected to proceed to first stage revision with removal of the prosthesis and joint debridement. The joint debridement in all cases involved extensive synovectomy, curettage of the acetabulum to bleeding bony surface and reaming of the acetabulum and femoral canals. Multiple specimens of the synovium, the acetabular capsule and pseudo-membrane of femoral and acetabular bone as well as femoral heads if present, were sent for microbiology and culture (minimum of 4-5 specimens from different areas). Jet lavage irrigation was carried out with at least 5 litres of normal saline. This was followed by placement of self-fabricated static cement spacers separately into the femur and acetabulum. The cement spacers that we fabricated were of two types: cement blocks (with Steinmann pin endoskeleton for the femoral spacer), and separate bolus of cement into the acetabulum (Figure 1).

The second type of spacer was antibiotic loaded cement beads on sturdy cerclage wires (Figure 2).

The process of fabrication of the antibiotic spacers were as follows. A sterile open bowl and a spoon were required. Into this bowl, each 40g of bone cement was admixed with 3.6g of tobramycin, 3g of vancomycin and 2g of cefazolin in powder form. If different antibiotics were used, it was important that they were of similar grouping to those above and were hydrophilic and heat stable.[5] Liquid antibiotics was not used as they do not mix uniformly in the cement.

The combined antibiotic and cement mixture was not vacuum mixed as it may impair antibiotic elution and may also aid cement interlock with bone by reducing porosity.[5] This antibiotic cement mixture when doughy was divided into 2 portions. One portion was wrapped around a Steinmann pin endoskeleton and placed in the reamed femoral canal, making sure that the spacer was not thicker than the last reamer. It should be placed in the canal just before it sets. The second portion was moulded into a ball and placed in the acetabular cavity (Figure 1). All cases had acetabular bone loss, so we elected to use static cement spacers.

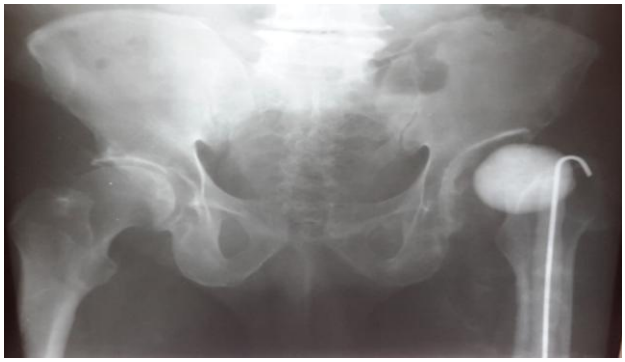

Figure 1: Static spacer blocks. Paprosky 2B acetabular defect. Femoral endoskeleton to aid removal of the cement spacer.

The other method of static cement spacer application was with self-fabricated cement beads. The bead maker was co-designed by one of the senior authors (TA). The antibiotic cement mixture as constituted above was placed into a bead maker containing a length of cerclage wire. It was then covered and secured until the cement was cured. The beads were removed and were applied into the femur and acetabulum (Figure 2).

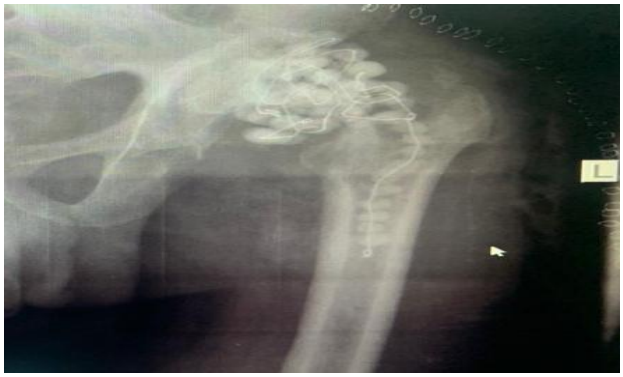

Figure 2: Cement beads in both the femoral canal and acetabulum. Noted is Paprosky 3A acetabular bone loss precluding articulating spacer application.

Following application of the spacer, the wound was closed in layers. No organisms were isolated in 5 of the cases presumably due to the prior use of over-the-counter antibiotics before presentation. Interval antibiotic treatment was guided by the microbiologists. High dose intravenous antibiotics were continued for 2 to 4 weeks depending on availability of peripheral veins, or the placement of a central venous line. If the inflammatory markers began to drop, it was followed by high dose oral antibiotics for a further 4 to 6 weeks with regular monitoring of the inflammatory markers and blood biochemistry to monitor for toxicity. When the inflammatory markers returned to normal, a 2-week antibiotic holiday was allowed, and the second stage revision was undertaken only when the inflammatory markers remained normal. If the inflammatory markers began to creep up during the antibiotic holiday, it was best to repeat the surgical debridement and the whole first stage process rather than persisting with antibiotic therapy or proceeding to second stage reconstruction. Inflammatory markers remained low and stable in all cases during the antibiotic holiday, and we proceeded to the second stage.

Following exposure and repeat debridement at the second stage acetabular and femoral bone loss were classified according to Paprosky acetabular bone defect classifications, to guide acetabular reconstruction. Noted were the following: Paposky 2 A in 1 patient, 2B in 1 patient, 2C in 2 patients, 3A in 4 patients and 3B in 2 patients.[4] These required bone grafts in 3 hips, Burch-Schneider cage in one hip and porous metal augment as a filler in 1 hip and porous metal augment as a buttress in another case. Porous trabecular metal shell was used in 2 hips. One femoral stem was cemented to ensure reduction in blood loss in the patient of the Jehovah Witness faith, who underwent hybrid total hip arthroplasty with trabecular acetabular shell (Figure 3). All other stems were cementless.

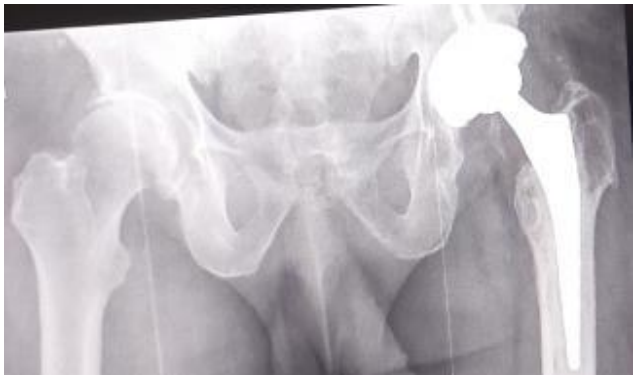

Figure 3: Post 2-stage reconstruction of case in Figure 1.

All cases underwent successful second stage hip reconstruction. Specimens taken at the second stage were further sent for microbiology and antibiotics were only stopped when the microbiology results following extended cultures were normal. There was no growth from specimens taken at the second stage in any case. Post-operative mobilization was individualised and dependent on the complexity of the case and stability of the reconstruction.

Patients are currently undergoing post-operative clinical, functional, and radiographic follow-up as per our arthroplasty registry protocol. This involves follow-up clinical assessment, X-rays, bloods including inflammatory markers, and functional assessments including Oxford hip scores.

DISCUSSION

There were 2 females and 4 males. Mean age was 40.5 years and range 24-60 years. Mean interval between the first and second stage was 8 weeks. One case has not undergone the second stage as he is unable to fund the operation. Organisms cultured include methicillin-sensitive *Staphylococcus aureus*, and *Enterococcus*. Mean pre-operative OHS is 16.6 (range 15-19) and post-operative OHS 43.7 (range 35-50). Mean post-operative follow-up 36 months (range 30-44 months). Radiologic assessment revealed that all implants were ingrown with intact interfaces in both cemented and cementless implants (Figure 3). There was no evidence of recurrent infection with all patients having well-functioning arthroplasties, no symptoms of infection and normalised inflammatory markers. Microbiology, acetabular defects and both pre-operative and post-operative OHS are shown in Table 1.

Total hip arthroplasty is an extremely successful surgical treatment for end-stage hip arthritis and is aptly called the operation of the century.[6] It results in excellent and predictable pain relief, restoration of function and improvement in quality of life.[7] Infection is however one of its commonest complication.[8] As more total hip arthroplasties continue to be undertaken, it is foreseeable that the incidence of prosthetic joint infection will continue to rise. In our environment, additional contributors to joint infections include infected hip hemiarthroplasties as well as native joint infections particularly in patients with sickle cell haemoglobinopathies.

The use of high eluting antibiotic cement spacer as part of the 2-stage treatment of prosthetic joint infection is well-established and can be extended to infected native hip joints particularly when the femoral head is diseased or destroyed.[9] The 2-stage treatment for prosthetic joint infection has high success rates of 90% in literature and is the gold standard treatment for prosthetic joint infections.[10]

Antibiotic loaded cement spacer application

Cement spacers can be prefabricated or self-fabricated by the surgical team intra-operatively. It can be articulating or non-articulating (static). It can also be classified into self-fabricated, moulded, prefabricated or antibiotic coated prosthetic spacers. It can be monolithic (hemiarthroplasty) or separate femoral and acetabular articulating coated implant spacer components.[2]

A bead-maker is required to make cement beads, and this is not widely available precluding its widespread use. The advantage of the cement bead as a spacer application is that the beads present a large cumulative surface area for local elution of antibiotics and potentially could achieve higher local antibiotic concentration than cement blocks. A study by Anagnostakos et al reported that cement beads were associated with 2 to 4 times higher antibiotic elution compared to cement blocks and antibiotic elution lasted longer.[11] This may make it more effective in eradicating infection when compared with cement blocks. Secondly the wire endoskeleton makes it malleable and able to be used to fill both femoral canal and acetabular cavities. The potential drawback of cement beads is that breakage of the wire can make retrieval of broken beads from the femoral canal a difficult and frustrating experience. It is therefore important when using cement beads to count and document in the operation note the number of beads in the femoral canal and the number of beads in the acetabulum to ensure complete removal of all beads at the second stage. Also, with use of beads as spacer the periarticular soft tissues cannot be tensioned as it can only be used as a static spacer.

A problem noted with our cohort of patients was the inability to culture organisms in 5 hips despite the presence of clinical and biochemical markers of infection. This was likely due to the prior use of non-prescription, over-the-counter antibiotics, a practice that is common in our environment. A crucial aspect in treating these cases is close collaboration with and guidance from infectious disease specialists (microbiologists). Empirical antibiotic selection is based on the underlying pathology such as sickle cell disease and knowledge of the bacteria that are commonly responsible for implant-associated infection locally.

Antibiotics mixed with cement for spacer fabrication are chosen based on the criteria outlined by Anagnostakos et al.[5] Commonly used combinations include vancomycin and tobramycin which provide coverage of wide spectrum of organisms including gram positive *Staphylococcus* (including methicillin resistant *Staphylococcus aureus* (MRSA) which are the most common cause of prosthetic infections.[10] Citak et al recommend addition of vancomycin (1-4g per 40g pack of cement) with either gentamycin or tobramycin (2.4-4.8g per 40g pack of cement) as spacer application, can treat most infections.[10] Furthermore, there is evidence for synergistic effect of both antibiotics in combination with the tobramycin improving the efficacy of the vancomycin.[5,12] We were successful in eradicating infection, reconstructing the joint and restoring function in all cases. We continue to monitor these cases regularly to ensure that there is no recurrent infection.

Native and prosthetic hip joint infections are not uncommon in patients with sickle cell haemoglobinopathy and failure of opsonisation that occurs in this disease predisposes patients to infection by capsidated organisms. The antibiotic regime including those used in the cement spacers appear to be effective for infections commonly

noted in this condition with all the 5 cases in our series successfully treated following the described 2 stage reconstruction.

Addressing the acetabular defects at the second stage

The commonest acetabular bone defect classification is the Paprosky classification which provides an indication of the severity of bone loss and guides treatment.[3] The detailed surgical management of major acetabular bone defect is beyond the scope of this article. We used bone autograft mixed with synthetic graft to address protrusion defects and trabecular metal augment as a filler for oblong 2B defects and as buttress augment for 3A defect. Burch-Schneider cage was used to reconstruct the more severe grades 2C and 3B defects. It is important to plan for reconstructing the acetabular defects based on the preliminary assessment during the first stage. With appropriate planning, it was possible to reconstruct most acetabular defects at the second stage.

Choice of spacer: pros and cons

In the presence of moderate to severe acetabular bone loss or when there is soft tissue incompetence, static spacers should be used. The cement spacer can be fabricated separately for the acetabulum and the femur. There is no risk of spacer dislocation or spacer fracture. It is cheap to make, and it is fabricated intra-operatively to fit the dimensions of each case. Furthermore, antibiotic choice and dose are at the discretion of the surgeon. Disadvantages include the inability to weight-bear in the interval between the first and the second stage. Also, soft tissue scarring and peri-articular contracture that results from static spacer use can result in difficulty in dissection during the second stage.[13]

It is important that in making the femoral block spacer a metal endoskeleton should be used as it makes for ease of removal. If a smooth Steinman pin is used, the ends should be bent as this ensures that the cement will be delivered, otherwise the pin may come out and the cement cylinder is retained and can be difficult to remove. If available, use of threaded pin as cement endoskeleton can help to deliver the cement when it is removed. An alternative static spacer is the antibiotic beads. This is malleable and can therefore be packed into both femoral and acetabular cavities. There is also evidence that the large cumulative surface area presented by the beads result in 2 to 4 times higher levels of antibiotic elution into the surrounding tissues.[5] A potential problem with beads is wire breakage and consequent difficulty with removal of retained beads. The use of thick wire endoskeleton can reduce this risk. It is important to count and record the number of beads placed so that they can be completely removed at the second stage.

If the acetabulum is congruent, with minimal bone loss, articulating spacers such as moulded or prefabricated hemiarthroplasty spacer with a metal endoskeleton or an articulating cement coated femoral component and loosely cemented polyethylene cup are preferred.[1] The advantages include the ability to partially weight bear and remain functional in the interval between the first and second stage. Also, maintenance of leg length and soft tissue tension allows easier second stage reconstruction due to preserved soft tissue planes and minimal soft tissue contracture.[1,13] Disadvantages include the risk of spacer dislocation, cement fracture and periprosthetic fracture around the spacer.[13] Furthermore, bone loss can occur if the spacer is ill-fitting and unstable. The prefabricated spacers, mold-derived spacers and cement coated implant spacers are expensive and not easily affordable as most patients pay out of pocket. Prefabricated spacers in our environment are almost 10 times more expensive than self-fabricated spacers. Most prefabricated spacers contain only low dose of a single antibiotic which may not provide bactericidal levels of local elution. If prefabricated spacers are used, it is important to make multiple drill holes in the spacer, fill these and cover the spacer surface with antibiotic cement mixture as described in this article.[15] This will increase the variety of antibiotics and increase the spacer surface area potentially making it more effective in eradicating infection.

Making articulating cement spacers with the use of molds are versatile but expensive.[14] Versatility derives from the ability to choose different femoral stem and acetabular molds to fit the specific femoral and acetabular geometries. In addition, neck offset can be adjusted to optimise interval periarticular soft tissue tension and joint stability. These spacers require separate femoral and acetabular molds to make them. Also, a separate cement gun is required for each mold. On average 3 to 4 bags of cement are required with 2 bags for the acetabular mold and one to two bags for the femoral mold. These are therefore expensive to make but provide the benefits of optimised soft tissue tension, hip stability, preserved tissue planes and ability to partially weight-bear if used.[13]

Antibiotic toxicity has also been noted to result from high antibiotic-loaded cement spacers including allergic reactions, nephrotoxicity, hepatotoxicity, and ototoxicity.[11,16] Renal and liver function should be monitored. Serum vancomycin levels should also be monitored.

We elected to undertake self-fabricated static cement spacers because all our cases presented with moderate to severe acetabular defects which precluded the use of articulating spacers. Scarring and contracture of soft tissues and blurring of soft tissue planes that can accompany the use of static spacers can potentially make the second stage reconstruction difficult.[11,13] We believe however that if infection is eradicated within 12 weeks of the first stage procedure, surgical exposure and identification of soft tissue planes is not particularly difficult, and we have not had any problems with exposing any of the joints during the second stage reconstruction.

We believe that the technique of self-fabricating static high antibiotic eluting cement spacer as part of the treatment of joint infection is a simple, safe, and cost-effective technique. It has a high chance of success in eradicating infection, and it is indicated when moderate to severe acetabular bone defect is present. It gives the surgeon control in the choice of the most effective antibiotic combinations and dosage that are likely to result in eradication of prosthetic infection including culture negative infections. The fabrication of spacers is based on the intraoperative canal and cavity dimensions of each individual case and spacers can therefore be made to size.

We have so far been successful in eradicating both native as well as prosthetic hip infections in all cases that presented to us using this technique and have obtained sound and functioning arthroplasties at early term follow-up. There is clearly a need for on-going and longer-term follow-up to continue to appraise the state and function of the joint.

CONCLUSION

We believe that self-fabricated, non-articulating (static), high eluting multi-antibiotic cement spacer is a cheap, easily manufactured antibiotic loaded cement spacer that has proved highly effective in eradicating both native and prosthetic joint infections including culture negative joint infections in our hands. We recommend this as a cement spacer option as part of a 2-stage procedure when faced with moderate to severe acetabular bone loss. It is effective in treating native or prosthetic hip joint infections including culture-negative infections and joint infections in patients with sickle cell haemoglobinopathy. When acetabular bone defect is minimal following debridement, articulating cement spacers should be used.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Ayekoloye CI, Balogun MJ, Alonge TO. Static antibiotic loaded cement spacer application in 2-stage management of native and prosthetic hip joint infections: a case series and review of the literature. Int J Res Orthop 2025;11:389-94.