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Two-stage revision of infected hip arthroplasty using a shortened post-operative course of antibiotics

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Abstract
Introduction We present a series of 30 consecutive patients with 31 infected total hip arthroplasties treated by a single surgeon over a 4-year period in whom a shortened post-operative course of antimicrobial chemotherapy was used.
Methods The treatment protocol consisted of a two-stage exchange with removal of infected components, insertion of an interim antibiotic eluting cement spacer and re-implantation of an extensively coated uncemented prosthesis on the femoral side. Systemic antibiotic treatment following each stage consisted of an abridged course of 5 days post-operative intra-venous administration followed by complete cessation of anti-microbial therapy.
Results At a mean follow-up of 35 months (minimum 24 months), there were no cases of recurrent prosthetic infection and no patient had required revision for aseptic loosening or mechanical instability on the femoral side. The combination of effective-staged surgical joint debridement, a shortened post-operative course of systemic antibiotic treatment and an adequate latent period before re-implantation has led to encourage early results in this series of revised chronic hip joint prosthetic infections.

Keywords Infection · Two-stage revision arthroplasty · Antibiotic · Cement

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Introduction

Periprosthetic deep infection after total hip arthroplasty (THA) is a devastating complication occurring with a frequency of approximately between 0.6 and 1% following primary THA [1–4]. The optimum surgical and pharmacological management of an infected hip endo-prosthesis remains a source of controversy. The central issues relate to staging of surgery, timing of prosthetic re-implantation and the dosage, duration and route of administration of antibiotics.

Although the relative merits of single versus staged revision have been well described [5], there is no current consensus regarding appropriate antibiotic regimes. A review of the recent literature reveals a wide array of different protocols ranging from no antibiotics [6–8] to courses of up to 9 weeks par-enterally, followed by oral therapy for varying periods [9–11]. This heterogeneity has implications with regard to costing, antibiotic side effect profile and toxicity, and timing of re-implantation. It is a potential confounding factor when interpreting the literature comparing single with staged revision surgery for infection.

It has been demonstrated experimentally that higher local tissue concentrations are achieved via elution from antibiotic laden bone cement than via par-enteral administration of antimicrobial chemotherapy. [12–14] In the majority of patients effective peri-prosthetic antibiotic levels are maintained for up to 4 months following implantation of antibiotic loaded cemented prostheses [14]. This may obviate the need for prolonged par-enteral and oral treatment.

We have adopted a protocol for the management of peri-prosthetic hip joint infection consisting of staged exchange of components, aggressive surgical debridement at each stage, insertion of an interim antibiotic eluting cement

spacer and administering an abridged course of post-operative par-enteral antibiotics. It is our impression that equivalent results are achieved with this regimen compared to others using longer durations of antibiotic treatment, conferring distinct advantages on both the patient and the institution treating him.

Patients and methods

This retrospective study analysed a consecutive series of patients presenting with infected hip endo-prostheses for treatment in our institution. Surgery was performed in all cases by the senior author (EM).

Patients attending with presumed peri-prosthetic hip joint infection are investigated in a standardised manner. A full history and clinical examination is performed, paying particular attention to the wound healing history, the current status of the hip wound and the presence of host factors that could predispose to infection. We record the number of previous surgeries on the same hip, time interval between primary THA and symptoms of infection. At presentation, baseline haematological parameters consisting of a full blood count, erythrocyte sedimentation rate (ESR) and c-reactive protein (CRP) are recorded.

In cases where the initial investigations raise the possibility of underlying infection, patients are scheduled for joint arthrography and aspiration.

All of the patients had at least one of the following: an organism cultured before open operation, a sinus communicating with the prosthesis, or purulent fluid at operation. Only patients with positive operative cultures were included in the study.

Deep infection in each patient was defined on the basis of time of onset and the clinical course as described by Fitzgerald. They were either Stage I, an acute fulminating infection developing within the first 3 months; Stage II, delayed sepsis developing as an indolent infection within the first 26 months; or Stage III, a possible haematogenous infection developing in a previously asymptomatic hip 23 months after arthroplasty [15]. Only patients with Stage II or III infection were included in the study.

In the absence of any factors mitigating against surgical treatment, all patients with established peri-prosthetic infection are scheduled for a staged debridement and exchange of components.

Based on the above criteria, we identified 31 consecutive two-stage revision arthroplasty procedures performed on 30 patients between 2001 and 2004. Seventeen patients were male and 13 were female. Their mean age was 63 years with a range from 38 to 76 years. The majority of patients (16/30) represented tertiary referrals having had their primary arthroplasty performed elsewhere. The implants had been cemented on both sides in 23 cases, uncemented in 4 cases and hybrid in 4 cases. The average interval between primary THA and revision for infection was 80 months and ranged from 6 to 324 months.

All had late chronic peri-prosthetic infection or haematogenous infection (Stages II and III as defined by Fitzgerald) [15]. The mean length of follow-up following two-stage revision was 36 months and ranged from 24 to 60 months.

Relevant host factors predisposing to the development of infection were present in seven patients. Three were type 2 diabetics. Two patients with rheumatoid arthritis had been on disease modifying immunosuppression. A further patient had been on immunosuppressive treatment for systemic lupus erythematosis. One patient had received systemic chemotherapy for ovarian cancer.

At the first stage, sinus tracts are excised and a radical joint debridement is performed with removal of the femoral and acetabular prostheses, cement and distal restrictors. On the femoral side, the extraction is facilitated using an extended trochanteric osteotomy (ETO), the length of which is determined by the extent of the distal cement to be removed.

After thorough irrigation of the operative field, an antibiotic-impregnated cement spacer is implanted. This consists of antibiotic mixed with Palacos® R cement. Each 40 g bag of Palacos R contains 80 mg of gentamycin premixed. In most cases, we use two bags (i.e. 160 mg gentamycin) and add 4 g vancomycin and 2.4 g tobramycin to the mix, unless pre-operative cultures dictate that other more suitable antibiotics may be used. Both vancomycin and tobramycin are available in sterile powder form and are heat stable. The spacer is hand moulded into the approximate shape of a hemiarthroplasty around a contoured intramedullary rod and implanted into the endosteal surface of the femur.

Each patient receives parenteral vancomycin for 5 days post-operatively, again unless previous cultures had identified that the bacteria were sensitive to a more appropriate antibiotic. Patients are allowed to toe-touch weight bear for the duration of the interval between stages.

As a simple investigation that can be performed and read in the clinic, we use the ESR and CRP to monitor the response to infection and to assist in scheduling of the re-implantation procedure. The second stage of the revision is performed once the CRP or ESR is returned to normal. Aspiration prior to re-implantation is not routinely performed.

At the second stage, a further radical debridement is performed. Tissue specimens were not routinely taken at this time. On the femoral side, an extensively coated porous uncemented prosthesis (Solution System®, DePuy Orthopedics, Warsaw, Indiana) is implanted with a Dall-Mile

Table 1 Organisms cultured from the 31 hips

Organism	Number
Staphylococcus aureus[a]	9
Staphylococcus epidermidis	15
Enterococcus	2
β-Haemolytic *Streptococcus*	3
Mixed culture[b]	2

[a] One case of *S. aureus* infection was MRSA

[b] The mixed cultures produced one patient with MRSA, and *Enterococcus* and another with *Staphylococcus epidermidis* and *β*-haemolytic *Streptococcus*

cerclage cable placed distal to the site of the extended trochanteric osteotomy. Reconstruction on the acetabular side is tailored to each case depending on the technical requirements encountered. Post-operatively, patients are treated with a further 5-day parenteral course of either vancomycin or the most appropriate antibiotic followed by a complete cessation of antimicrobial therapy.

They were followed up at regular intervals and assessed for pain, range of motion, wound healing, Harris hip scores, radiographs, ESR, CRP and full blood counts (FBC). Aspiration of the joint at follow-up was not routinely performed. If the patient demonstrated persistent pain, X-ray signs of loosening or infection, or persistently raised inflammatory markers, then they would be investigated accordingly with bone scan and/or aspiration to out-rule recurrent infection.

Results

Preoperative investigations

The mean preoperative ESR was 58 mm/h (6–100 mm/h) and the mean CRP was 32 mg/l (6–62).

Aspiration was performed in 25 of the 31 hips. Eighteen of the aspirations grew an organism. Intraoperative cultures taken from these patients matched the aspiration organism in all cases where both were available. Revision surgery went ahead in the remainder based on clinical and radiological findings. Results of the aspiration organism and intraoperative samples are shown in Table 1. There were two multiple infections. One grew MRSA and *Enterococcus*, and the other grew *β*-haemolytic *Streptococcus* and *Staphylococcus epidermidis*. *Staphylococcus epidermidis* was the most common organism. Five patients had a chronic discharging sinus.

The pre-operative X-ray appearances are summarised in Table 2. All but 12 had loosening of at least one component. The appearances were not specific to infection in the majority of cases.

Table 2 Preoperative X-ray findings

X-ray findings	Number of cases
Radiolucent acetabular component	13
Radiolucent femoral component	11
Periosteal femoral reaction	2
Nonunion of femoral fracture	1
Dislocation acetabular cup	1

Course of treatment

Hospital stay after the first stage was an average of 16 days (range 7–27). Although all were on parenteral antibiotics for only 5 days, some needed extended hospitalisation to adequately control pain or else had extenuating home circumstances negating our ability to discharge.

In all but five patients the antibiotic regime added to the cement consisted of tobramycin and vancomycin. Four of these patients received vancomycin only and one received vancomycin plus 1 g of gentamycin in addition to the gentamycin already present in the bone cement. These alterations were based on advice from microbiological sensitivities. The post-operative antibiotics administered were intra-venous vancomycin in all but six cases. The antibiotics used in these cases were intravenous gentamycin in combination with oral rifampicin (two cases), vancomycin in combination with rifampicin (two cases), vancomycin in combination with oral linezolid (one case), and IV gentamycin alone (one case). These regimes were all based on microbiological advice.

The second stage was attempted when the patient's ESR fell to less than 20 mm/h. The interval between stages was on average 16 weeks with a range of 3–31 weeks. The delay in most cases was due to a persistently high ESR. There were two cases where stage II commenced before normalisation of the ESR. One was in a patient with severe learning difficulties and repeatedly dislocated her temporary prosthesis. The other was a patient who developed a periprosthetic fracture of her femur around the temporary prosthesis and required stage II to be attempted at 3 weeks.

An extensively coated uncemented revision stem (Solution System®, DePuy Orthopaedics) was used in all but one case. The one exception was a case where a Charnley prosthesis was cemented into the femur.

Eleven of the patients had the acetabular side augmented with impacted fresh frozen allograft as there was a significant bone defect. A polyethylene cup was cemented into this using antiobiotic impregnated polymethylmethacrylate cement (Palacos R). An uncemented Mallory cup (Biomet Inc, Warsaw, Indiana) was impacted into the acetabulum of the remaining 20 patients.

Mean hospital stay after stage II was 13 days (range 8–22).

Table 3 Harris hip scores

	Average Harris hip score (95% CI)	Range
Pre-revision	45 (41.8–48.1)	32–62
Post-revision		
3 months	81 (78.4–84.2)	54–91
24 months	93 (86.9–99.6)	79–100

Complications

There was one mortality in our study and this was not related directly to the infection. He passed away 14 days after stage I from a bleeding duodenal ulcer. Stage I morbidity included 7 patients: two sustained excessive blood loss requiring greater than 6 units of blood transfusion. Two periprosthetic fractures of femurs occurred post-operatively while the patients attempted mobilisation in the interim period. One developed a urinary tract infection and another dislocated their temporary prothesis. Morbidity after stage II was limited to two patients requiring blood transfusions of more than 6 units, two urinary tract infections and one case of pneumonia.

Five patients dislocated their revision THA within 6 months following reimplantation. Two became persistent dislocators. The first is mobilising with a chronically dislocated prothesis and the second required a girdlestone arthroplasty to be carried out.

Outcome

At a mean follow-up of 35 months (range 24–60 months), there were no cases of re-infection.

Harris hip score were recorded prior to revision procedures and post-operatively at 3 months and 2 years by our joint registry. Of the original 30 patients included in the study, data was recorded in 28. The two patients excluded were the patient who underwent a girdlestone arthroplasty and the patient who remained permanently dislocated. A significant improvement was seen between the pre-operative and 3 months post-operative scores (student's independent t test, $P < 0.001$) and also between the 3 months and 2 year post-operative scores (student's independent t test, $P = 0.001$; Table 3).

Discussion

The management of peri-prosthetic infection places significant demands on the resources and finances of an institution [16]. Physical and psychological effects on the patient are considerable. The principal aims of treatment are to eradicate infection and restore function to the patient. In the setting of established infection, where implant exchange is required, it has been our protocol to use a two-stage revision procedure with placement of an interim antibiotic eluting cement spacer. We believe it provides a more optimum environment for the eradication of infection than direct exchange procedures. In addition, staged revision for infection allows for uncemented reconstruction and allograft augmentation to be carried out with greater confidence [7, 11, 17]. In a meta-analysis of 12 studies examining the results of two-stage revision for infection using an interim antibiotic impregnated cement spacer, the cumulative rate of eradication of infection was 91% (385 of 423 hips). This compared favourably with a success rate of 82% (976 of 1,189) in treating hip joint prosthetic infection using direct exchange with antibiotic loaded cemented implants [18].

The rationale for using an abridged course of par-enteral antibiotic is due to the effective and sustained elution of antibiotic from the cement spacer into local tissues. Although there is a time dependent decline in achieved tissue concentrations, a number of studies have demonstrated maintenance of antibiotic levels above the minimum inhibitory concentration of common pathogens for several months following implantation [14, 19–21]. A shorter duration of par-enteral treatment lessens the likelihood of systemic toxicity and may result in a reduction in the emergence of drug resistance organisms [14, 22–24]. In the presence of infection and surgical trauma, it is known that tissue blood supply may become attenuated, thus limiting the levels of systemically administered antibiotic reaching the desired site of action [25].

Typically, recommendations for the duration of par-enteral antibiotic treatment following revision for infection range from 4 to 6 weeks. A wide variety of treatment durations have been reported [2, 7, 26–33]. There has been some evidence to date that shorter courses may suffice. Hoed-Reddick et al. reported a success rate of 89% in eradicating infection during staged revision in the setting of infected total knee arthroplasty in a series of 53 patients using only 24 h of intravenous cefuroxime [34]. However, the complete elimination of parenteral antibiotics is not advisable. Using single stage revision without antibiotics, Buchholz et al. reported a 23% re-infection rate. Ammon and Stockley reported recurrence of infection in 14% of cases (8 out of 57) following staged revision for infection without the use of systemic antibiotics in patients requiring impaction allografting as part of their reconstruction [7].

In general, we chose to use a combination of three antibiotics impregnated into our cement spacer. Bacteriocidal antibiotics used in combination has been shown to improve eradication and reduce the development of resistant strains. Some bacteria, in particular, staphylococci rapidly develop resistance, therefore one single antibiotic should never be used [35]. Three antibiotics reduce the chance that the

organism is resistant and reduces its ability to develop further resistance.

More recently, this same group has published their data in 114 patients who underwent a two-stage revision with the use of antibiotic-impregnated cement beads and only 24 h of intravenous antibiotic prophylaxis [8]. They were able to achieve success in 87.7% of their patients with a minimum follow-up of 2 years. They concluded that the combination of the radical debridement and implantation of antibiotic-laden cement beads achieves similar levels of success as that by prolonged courses of antibiotics. Although similar to our study, there were some significant differences. Whereas they used vancomycin only in biconcave cement beads, we used a combination of tobramycin and vancomycin in the cement contoured as a spacer. We believe the spacer preserves the soft tissue tension and improves the interim function of the hip and mobility of the patient leading to a shorter hospital stay. We also used 5 days of IV antibiotics. The rationale of this was to eliminate any bacteria which was displaced from the surgical area, not removed at debridement, or otherwise was not in close proximity to the cement spacer.

Our series represents a retrospective review of consecutive patients treated by a single surgeon. We believe the most critical aspect of treatment of infected hip arthroplasty is the extent of the radical debridement. This is a difficult factor to account for in any single surgeon series. The extent of the debridement needed is an intra-operative judgement based on the surgeon's experience and willingness to remove potentially infected tissue. Until a unit with multiple surgeons adopts a shortened course of intravenous antibiotic administration post two-stage revision, it will be difficult to make any definitive statements as to its success.

Furthermore, because this series is a retrospective analysis, it represents a relatively low level of evidence. A randomised controlled trial would provide a greater understanding of the advantages of this particular method of revision for infected hips.

In the present series of 31 infected hip arthroplasties treated in 30 consecutive patients, there has been no case of recurrent infection to date. Strict adherence to the principles of surgical debridement and a rationalisation of the route of administration and duration of antibiotic treatment has led to the development of a simplified and easily followed regimen for this often complex problem. These preliminary results, we believe warrant further investigation.

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