Is there a role for extended antibiotic therapy in a two-stage revision of the infected knee arthroplasty?

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All major studies have incorporated the use of prolonged courses of parenteral or oral antibiotic therapy in the management of two-stage revision of an infected total knee arthroplasty. We present a series of 59 consecutive patients, all with microbiologically-proven deep infection of a total knee arthroplasty, in whom a prolonged course of antibiotic therapy was not routinely used. The mean follow-up was 56.4 months (24 to 114).

Of the 38 patients who underwent a staged exchange, infection was successfully eradicated in 34 (89%) but recurrent or persistent infection was present in four (11%). Our rate of cure for infection is similar to that reported elsewhere. We conclude that a prolonged course of antibiotic therapy seems not to alter the incidence of recurrent or persistent infection. The costs of the administration of antibiotics are high and such a regime may be unnecessary.

Deep infection remains a difficult problem after knee replacement surgery and rates between 0.5% and 2% have been reported.¹⁻³ Increased rates of infection are encountered in knees which have undergone many operations and in patients with other medical comorbidities.^{4,5} Treatment of an infected knee arthroplasty is controversial with many protocols being described. Each has its advocates with options which include arthroscopic wash-out,⁶ open debridement with exchange of polyethylene⁷ and a staged exchange of components.⁸ The last approach may include the use of antibiotic spacers, with subsequent reimplantation when soft tissues permit and infection appears to have been eradicated. This two-stage approach is perhaps the method of choice with reported rates of control of infection in the region of 90%.⁹ All major studies reported to date have involved the long-term administration of antibiotics between the stages,⁹⁻¹¹ and more recent series have also included the use of antibiotic impregnation of the cement spacer.^{10,12-14} Antibiotics are often delivered intravenously which frequently requires a lengthy inpatient stay and placement of a central venous catheter. The costs both to the patient and the health care facility are high.^{15,16}

In our unit, we use a two-stage approach with radical debridement, the insertion of an antibiotic-impregnated cement spacer and antibiotic-loaded beads at the first stage. Pro-

longed courses of antibiotics have not been routinely used. We now report an analysis of all the patients treated by a two-stage reconstruction for infection of a total knee arthroplasty under the care of the senior author (IS).

Patients and Methods

Between 1992 and 2001, a two-stage reconstruction in 59 patients with suspected deep infection of a total knee arthroplasty was undertaken. These patients have been prospectively followed up every year both clinically and radiologically according to our policy. We defined infection as multiple, positive microbiological samples obtained either at aspiration or at first-stage debridement. No microbiological evidence of infection was identified in six patients and these were therefore excluded, leaving 53 with definite infection.

There were 27 women and 32 men with a mean age at presentation of 70.6 years (34.8 to 87.1). Comorbidity was common, with nine patients having diabetes mellitus. Two required dialysis for chronic renal failure and one had hypophosphataemic rickets. Six had rheumatoid arthritis, one had psoriatic arthritis and the remainder had osteoarthritis.

Aspiration was performed on all patients before the first-stage debridement and the results were interpreted by a microbiologist (PN) with an interest in prosthetic infection. The antibiotics were stopped at least two weeks before the aspiration.

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At the first stage, the antibiotics were withheld until multiple tissue specimens had been taken. After removal of the components and all cement, the bone and soft tissues were radically debrided. Restoration of the soft-tissue envelope had a high priority, with plastic surgery being undertaken at the time of the first stage when necessary.

In order to provide stability, maintain the joint space and supply antibiotics, a polymethylmethacrylate spacer was prepared at the time of surgery. Additional antibiotics were added to the cement as indicated by the culture results at pre-operative aspiration. Increased local elution of antibiotics was achieved by fashioning cement beads, again with additional antibiotics, a method which has been shown to give higher concentrations of antibiotic locally than are achieved by the administration of intravenous antibiotics.¹⁷ The customised cement beads and spacer were tailored to the microbiological findings. When either vancomycin or gentamicin was indicated, 2.0 g of vancomycin or 1.0 g of gentamicin were added to each 40 g mix of Palacos R cement (Schering Plough Ltd, Welwyn Garden City, UK). When required, additional stability was obtained by the use of an intramedullary nail of narrow diameter coated in cement.

A broad-spectrum antibiotic, typically cefuroxime (1.5 g at induction and two further doses of 750 mg at eight and 16 hours post-operatively), was given intravenously as surgical prophylaxis. No additional oral or intravenous antibiotics were given routinely. The patients were mobilised, weight-bearing as tolerated, and were discharged home when their wound was dry and they had adequate mobility.

Outpatient monitoring included clinical examination and assessment of inflammatory markers. When the soft tissues were quiescent and serological markers were satisfactory (CRP < 10 mg/l, ESR < 20 mm/hour), the patients were considered for a second-stage reconstruction.

At re-implantation multiple specimens were again collected for microbiological analysis and the same regime of antibiotic prophylaxis was used. The results of cultures from the first stage determined what antibiotics, if any, were added to the cement which was used for the fixation of the components.

The mean number of surgical procedures performed before presentation to our unit was 1.9 (1 to 8). Eleven patients had already undergone multiple revision procedures, with a mean of four procedures (2 to 8).

Twenty-nine patients (49%) presented with open, purulent wounds, discharging sinuses or frank formation of an abscess. In order to achieve a stable, well-vascularised soft-tissue envelope, nine patients required plastic surgery.

Results

Thirty-nine patients underwent a staged re-implantation of their total knee arthroplasty. A formal two-stage arthrodesis was performed in five in whom the quality of the soft-tissue envelope was considered to be too poor for prosthetic reimplantation, despite having had plastic surgery, or when

Table I. Organisms responsible for infection

Organism*	Frequency	Antibiotic added to cement
CNS ^R	4	Vancomycin and gentamicin
CNS ^S	9	Gentamicin
<i>Staphylococcus aureus</i>	5	Gentamicin
MRSA	1	Vancomycin and gentamicin
<i>Enterococcus</i> ^S	3	Vancomycin and gentamicin
<i>Enterococcus</i> ^R	3	Vancomycin
Streptococci	2	Vancomycin and ampicillin
<i>Pseudomonas</i>	1	Gentamicin
<i>Propionibacterium</i>	2	Vancomycin and gentamicin

*CNS, coagulase-negative *staphylococcus*; ^R, gentamicin-resistant; ^S, gentamicin-sensitive; MRSA, methicillin-resistant *Staphylococcus aureus*

the extensor mechanism was found to be inadequate. Nine had a debridement and implantation of a cement spacer for infection but were either considered to be too unfit for, or declined, further surgical reconstruction. One underwent an above-knee amputation after a vascular injury which occurred during their second-stage re-implantation and has therefore been excluded from the results relating to infection. A total of six patients who had further surgery, reconstruction or arthrodesis, required a further debridement before reimplantation. Two of these needed a total of three debridements before definitive re-implantation. The median interval between the stages was 24 weeks (4 to 64).

The mean follow-up after the second stage was 56.4 months (24 to 114). A total of 44 patients underwent a staged procedure. All had microbiologically-confirmed deep infection. In 30 (68%) a single organism was identified (Table I), whereas in the remaining 14 (32%) there was more than one infecting organism. Three of these patients were infected by three different organisms. The most commonly encountered organism in this group was coagulase-negative staphylococcus (CNS). This was isolated in 11 of the 14 patients. The incidence of sinuses was also high in this group (eight of 14 patients). No organisms were grown from second-stage samples in 37 patients (84%) but seven (16%) had positive samples from the second stage (Table II).

Of the 38 patients, one being excluded as a consequence of above-knee amputation, who underwent a staged exchange, infection was successfully eradicated in 34 (89%) but recurrent or persistent infection appeared in four (11%) (Table III). These patients could be divided into two groups, those infected by a single organism and those with an infection which was caused by more than one organism. Twenty-five (96%) of the 26 patients who were infected by a single organism were treated successfully by this regime. In the 13 patients with more than one organism, recurrent or persistent infection was seen in three. This gave a rate of success for the eradication of infection of 77%.

Of the five patients who underwent a staged arthrodesis, all had negative cultures at the time of their fusion. We achieved a successful fusion, with eradication of infection, in four (80%). The remaining patient, who required a local

Table II. Positive cultures identified at the second stage

Case number	Original organisms*	Second-stage organism*	Result
2	CNS ^R	CNS ^R	Recurrent infection, treated by washout and antibiotic suppression
5	<i>Enterococcus</i> ^S	<i>Enterococcus</i> ^S	Success
8	CNS ^S	CNS ^S	Success
15	CNS ^R and <i>enterococcus</i>	<i>Propionibacterium</i>	Success
19	<i>Enterobacter</i> , <i>Enterococcus</i> ^R	<i>Enterococcus</i> ^R	Success
22	<i>Enterococcus</i> , <i>Proteus</i> group-B haemolytic streptococcus	<i>Propionibacterium</i>	Success
34	CNS ^S , <i>Streptococcus viridans</i>	CNS ^S	Success

* CNS, coagulase-negative *staphylococcus*; ^R, gentamicin-resistant; ^S, gentamicin-sensitive

Table III. Patients with recurrent infections

Case number	Comorbidity	Sinuses	Original organism*	Second-stage culture	Recurrent organism*	Outcome
2	None	Yes	CNS ^R	CNS ^R	Unknown	Antibiotic suppression
3	Five earlier procedures; infected revision	Yes	<i>Candida</i> , CNS ^S , Diphtheroids	Sterile	CNS ^R , <i>Enterococcus</i>	Amputation
4	None	No	CNS ^S , Diphtheroid, <i>Propionibacterium</i>	Sterile	Unknown	Antibiotic suppression
6	Diabetic	No	CNS ^R , <i>Staphylococcus aureus</i>	Sterile	<i>Enterobacter</i>	Amputation

* CNS, coagulase-negative *staphylococcus*; ^R, gentamicin-resistant; ^S, gentamicin-sensitive

gastrocnemius flap, had a loose intramedullary nail on review. The previous infection was caused by a species of *Enterococcus*. A repeat aspiration isolated CNS and further surgery is planned.

Discussion

This is a consecutive series of microbiologically-confirmed infected knee arthroplasties managed by a single surgeon. As with other series, multiple operations and medical comorbidities were commonplace. Other series of similar patients have reported comparable results for the eradication of infection but all have used long-term antibiotic therapy, either oral or intravenous, which has ranged in duration from six weeks to 16 months. In our series, long-term antibiotic therapy was not routinely used. The mean duration of intravenous therapy of 4.64 days (1 to 7). Only three patients in the successful groups required further courses of oral antibiotics. One patient needed a course of flucloxacillin for six weeks between the first and second stages in order to provide antibiotic cover for plastic surgery (tissue expansion). Two patients took oral ampicillin after their second-stage reimplantation, for five days and six weeks, respectively since their original infecting organisms included a high-level gentamicin-resistant *Enterococcus*.

Repeat debridement was required in six of the 44 patients. Two required a total of three debridements before re-implantation. A high incidence of pre-operative sinuses was seen in these patients; four sinuses in six patients. Infection by multiple organisms was associated with a poor outcome (Table III).

We, therefore, suggest that prolonged courses of antibiotics may be unnecessary provided that a rigorous

debridement is performed and microbiological advice is followed regarding the addition of appropriate antibiotics to the cement at the appropriate stages. We use custom-made antibiotic beads to deliver a high local concentration of antibiotic to the bone and soft tissues. These are used in addition to an antibiotic-impregnated cement spacer. The available surface area of the beads is greater than that of a spacer and therefore allows a larger dose of antibiotic to be eluted from them. By employing this protocol we have shown comparable results with those of other series, all of which used prolonged courses of antibiotic therapy in addition to surgical debridement and antibiotic-loaded cement spacers.

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