The use of vancomycin-impregnated cement beads in the management of infection of prosthetic joints
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Although the incidence of infection associated with hip and knee prostheses is low, with the increasing number of arthroplasties being carried out, the total number of such cases is increasing. The pattern of infecting organisms after total joint arthroplasty has changed and gentamicin-resistant organisms are becoming increasingly common. In conjunction with surgical debridement, vancomycin added to a bone-cement carrier can be very effective in the treatment of infection caused by such organisms.

We report the results of its use in proven deep infection in 26 hip and seven knee arthroplasties. After a mean follow-up of 67 months, 32 patients remained clinically and radiologically free from infection. There was one recurrence and positive second-stage cultures of uncertain significance in three other patients. Vancomycin is potentially very useful in the management of deep infection after arthroplasty.

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Although there has been considerable progress in reducing the incidence of deep infection after arthroplasty, it remains a potentially devastating complication.1 Exchange arthroplasty using either one- or two-staged procedures with gentamicin-impregnated bone cement has produced good results, with microbiological cure in approximately 90% of cases. Unfortunately, the pattern of organisms causing sepsis has changed, partly as a result of prophylaxis with local and systemic antibiotics. In many centres, coagulase-negative staphylococci (CNS) are now responsible for most cases of deep infection2,3 and many strains of CNS are resistant to gentamicin. Vancomycin (Lilly Industries Ltd, Basingstoke, UK) is heat-stable and known to elute from polymethylmethacrylate (PMMA) cement. Our aim was to evaluate clinically the efficacy of vancomycin-impregnated PMMA cement in the management of deep infection.

Patients and Methods

Between 1992 and 1996, we identified 33 patients, 16 men and 17 women, with chronic infection of a prosthesis due to gentamicin-resistant organisms. There were 26 hips and seven knees. The mean age of the patients was 73.9 years (44 to 84).

After clinical and radiological assessment, all patients underwent aspiration of the joint under general anaesthesia in a laminar-flow theatre to identify the infecting organism. The specimens obtained were inoculated directly on to two blood agar plates, one incubated aerobically with CO2 and the other anaerobically. They were also inoculated into brain-heart infusion broth and fastidious anaerobe broth. All specimens were incubated for seven days, examined daily, and subcultured on to blood agar plates, as above, if there was any suspicion of growth. After seven days, terminal subculture was undertaken.

After confirmation of deep infection with gentamicin-resistant organisms, the patients were managed by a two-stage exchange procedure. At the first stage, a thorough debridement was carried out with excision of dead and infected tissue and removal of the prosthesis and all cement and foreign material. Multiple tissue samples were taken for further microbiological analysis before systemic antibiotic therapy was administered. Immediately after the tissue samples had been taken, the patients were given intravenous cefuroxime (750 mg three times daily) provided that they were not allergic to it. This continued for five days after operation. Systemic antibiotics were given as prophylaxis against further potential infection rather than for treatment of the established infection, since our treatment regime was essentially surgical with radical debridement and the introduction of high-dose antibiotic depots.

After the debridement, antibiotic-loaded methylmethacrylate cement beads were prepared by adding 2 g of vancomycin powder to a 40 g pack of Palacos R cement (Schering-Plough Ltd, Welwyn Garden City, UK). The
cement was formed into the shape of bioconcave discs and held on 18-gauge braided wire to form chains. These were then inserted into the acetabulum and femoral canal, before wound closure over suction drains.

In some patients with mixed infections, antibiotics in addition to vancomycin were added to the bone cement.

A total of 31 patients had second-stage reconstruction with reimplantation of a prosthesis after a mean of 9.2 months (2 to 36). One patient with an inadequate extensor mechanism had a knee arthrodesis and the remaining patient declined further surgery.

All the patients were reviewed at three, six and 12 months after surgery and then annually. No patient was lost to follow-up. The mean follow-up was 66.8 months (60 to 112). The 32 who had reconstructive surgery were reviewed clinically, radiologically and haematologically with measurement of the ESR. The level of the ESR was classified as normal (less than 20 mm/hour), high (20 to 80 mm/hour) or very high (over 80 mm/hour). The trends in the ESR were classified as follows: grade 1, high or very high, returning to normal; grade 2, very high which decreases but still remains high; grade 3, high or very high which remains unchanged; grade 4, normal which remains unchanged; grade 5, rising from high to very high; and grade 6, rising from normal to high or very high.

Results

The microbiological results of the tissue specimens taken at the first-stage procedure were regarded as definitive and showed agreement when compared with those obtained from the joint aspiration. In two patients, gentamicin-resistant organisms were grown from the biopsies, but not from the multiple specimens taken at the first stage. In another patient, a gentamicin-resistant diphtheroid was grown in all the first-stage operative specimens, but not from the aspiration. The reason for these discrepancies was uncertain, but false-positive and false-negative results have been recognised in most reported series of infected arthroplasties. The infecting organisms cultured from the first-stage procedure are shown in Table I. The minimum inhibitory concentrations of gentamicin for all the identified organisms was estimated and confirmed that gentamicin in the Palacos R cement could not have been effective in eradicating the infection.

Second-stage surgery provided an opportunity for further microbiological analysis. The results of multiple specimens taken from the 31 patients who had a prosthesis reimplanted are shown in Table II. Three patients had positive second-stage cultures. One grew gentamicin-resistant CNS; after eight years there was no evidence of clinical or radiological failure and the patient had a low ESR. The other two patients grew high-level gentamicin-resistant Enterococcus faecalis. One was given long-term oral ampicillin. After three years the antibiotics were stopped and eight years after reimplantation she remains well, without clinical or radiological evidence of infection and with a normal ESR. The remaining patient was treated with intravenous amikacin for six weeks after the second-stage cultures revealed persistent infection. There were no signs of failure after six years and the ESR was low.

One patient had recurrence of infection four years after reimplantation. At the second stage all the operative cultures were sterile. Repeat aspiration revealed gentamicin-sensitive CNS, which could have been a new infection from the reimplantation or a recurrence of the original mixed infection. In the other 28 patients there was no growth from the multiple specimens taken at the second stage, which is suggestive of microbiological cure.

Two patients died from unrelated causes. At their last review 65 and 67 months after surgery there was no clinical evidence of joint failure and the ESR was normal.

No formal scoring system was used for clinical assessment but all except the patient with a continuing infection, had satisfactory function and clinical results. Improvement in pain was universal and significant. Radiological signs of loosening almost invariably preceded the clinical evidence and despite annual radiological follow-up there was only one case of loosening, in the patient with recurrent infection.

With regard to the ESR one patient was classified as grade 6, two as grade 4, three as grade 3, four as grade 2 and 20 as grade 1. There were no grade-5 patients. In the remaining three patients there was no adequate information to assess accurately the trend in the ESR and these patients were not classified.

Discussion

Gentamicin-impregnated bone cement has been in clinical use for nearly 30 years with proven results in the management of infection of a prosthesis. The concentration of

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### Table I. The organisms cultured from the 33 patients at the first stage of revision arthroplasty

<table>
<thead>
<tr>
<th>Organism cultured</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resistant CNS</td>
<td>21</td>
</tr>
<tr>
<td>Resistant CNS + Enterococcus faecalis</td>
<td>4</td>
</tr>
<tr>
<td>Resistant CNS + Staphylococcus aureus</td>
<td>2</td>
</tr>
<tr>
<td>Resistant CNS + Escherichia coli</td>
<td>1</td>
</tr>
<tr>
<td>E. faecalis</td>
<td>2</td>
</tr>
<tr>
<td>E. faecalis + Pseudomonas</td>
<td>1</td>
</tr>
<tr>
<td>E. faecalis + Enterobacter</td>
<td>1</td>
</tr>
<tr>
<td>Resistant diphtheroid</td>
<td>1</td>
</tr>
</tbody>
</table>

### Table II. The organisms cultured from the 31 patients at the second stage of revision arthroplasty

<table>
<thead>
<tr>
<th>Organism cultured</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>28</td>
</tr>
<tr>
<td>Resistant CNS</td>
<td>1</td>
</tr>
<tr>
<td>High-level-resistant E. faecalis</td>
<td>2</td>
</tr>
</tbody>
</table>
antibiotic eluted from the cement is much greater than that which can be achieved by systemic therapy. Local antibiotic depots can sterilise an adequately debrided joint and avoid the need for prolonged intravenous administration. Palacos R has been shown to have more favourable elution characteristics when compared with other PMMA bone cements.\(^5,6\) The rationale for using vancomycin in our patients was its known efficacy against the infecting organism and its suitable characteristics for use in a bone-cement carrier. It is heat-stable and has been shown to have satisfactory elution characteristics with high local concentration for a number of days\(^7,9\) and a potentially higher antimicrobial activity when compared with gentamicin.\(^10\) We had no reported cases of allergy, toxicity or intolerance which is comparable with another series.\(^9\) While antibiotics other than gentamicin have been used in a number of centres and vancomycin is utilised elsewhere\(^11\) we found no other reports of the results of its use in the English literature.

Recurrence of deep infection is most likely to occur within 12 months of revision surgery.\(^12\) The minimum follow-up for all our patients was 60 months.

Only one failure was identified and the two deaths which occurred were after five years. Vancomycin-impregnated cement in the form of beads appeared to be a very effective adjunct in the management of chronic infection after arthroplasty.

While the ESR is a non-specific parameter, its use in monitoring infection in a joint has been well documented, as have its limitations.\(^13,14\) There may be other reasons for a raised ESR in patients undergoing exchange arthroplasty such as inflammatory arthropathy and other chronic diseases. Since 20 of our patients had an ESR which was high or very high before surgery, but which subsequently returned to normal, this must be regarded as very encouraging. In a further four patients the very high ESR had fallen significantly, but remained high. Of the three patients in grade 3, in which the ESR was high or very high and remained unchanged despite revision surgery, two had concomitant underlying rheumatoid arthritis. The two patients who always had a normal ESR were the youngest.

The theoretical rationale for using vancomycin would appear to be substantiated by its clinical efficacy. Its use in patients who had infections with high-level gentamicin-resistant Enterococcus faecalis must be questioned, since the two patients in our series still had positive second-stage cultures and subsequently had additional therapy with other antibiotics. Despite the fact that there was no evidence of the recurrence of infection in these two patients vancomycin could not be presumed to have been effective. Apart from these two patients it would seem that there is a definite place for using vancomycin beads if an antibiogram obtained from cultures after biopsy shows resistance to gentamicin and sensitivity to vancomycin. The use of such beads would appear to be useful in the treatment of infection of a joint prosthesis.

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References