Gentamicin release from old cement during revision hip arthroplasty

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Bone cement containing gentamicin may release antibiotic when fractured during revision operations. Tissue samples taken during surgery may be contaminated by gentamicin and give inaccurate microbiological assessment.

We studied five patients in whom cement containing gentamicin had been used in the primary procedure. During revision hip replacement, samples of joint fluid, tissues and cement were taken both before and after disruption of the cement.

With the exception of one sample of joint fluid, low concentrations of gentamicin were recorded in the samples taken before the cement was disrupted, but after disruption the specimens contained gentamicin at concentrations high enough to inhibit or prevent growth of sensitive organisms. The cement contained very high levels up to ten years after insertion.

Our findings suggest that no reliance can be placed on the microbiological assessment of specimens taken once cement splitting has started and that specimens should therefore be taken as early as possible.


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Since the 1970s the benefits of using acrylic cement containing gentamicin to minimise the risks of infection in hip arthroplasty have been well accepted. Its widespread use, along with clean-air technology and parenteral antibiotics, has considerably reduced rates of infection. In the USA, it is estimated that up to 88% of surgeons use bone cement impregnated with antibiotic1 and this is also probably the case in Europe.

One of the most serious causes of loosening after hip replacement is infection which may jeopardise the success of a revision procedure. Deep infection may not always be clinically obvious and various investigations, including microbiological analysis, often have to be undertaken. Awareness of infection by multiple strains or multiple pathogens is essential as is knowledge of acquired gentamicin resistance in some strains of coagulase-negative Staphylococcus2.

Many patients who now require a revision procedure are likely to have received bone cement containing gentamicin at their primary operation. There has been speculation that disruption of this cement during a revision procedure could release the gentamicin into the surrounding tissues,3 and lead to difficulty in the culture of certain pathogens.

Our aim was to determine if significant levels of gentamicin are present in samples of tissues taken routinely for microbiological analysis during revision hip arthroplasty when cement containing gentamicin is being removed.

Patients and Methods

Tissue samples were taken before and after the bone cement was damaged from five consecutive patients having revision hip arthroplasty, in whom it was known that cement containing gentamicin had been used in the primary procedure. The samples, from the joint fluid or blood, joint capsule and membrane or granuloma, are those taken routinely at operation in cases of suspected deep infection. The concentration of gentamicin was measured in these samples, and in samples of cement. A routine operation was then carried out.

The Bristol Centre for Antimicrobial Research and Evaluation at Southmead Hospital assayed the supernatant from the fluid samples and aqueous extracts from thinly sliced tissues and crushed bone for gentamicin using the Abbott TDx system (Abbott Laboratories, Chicago, Illinois).

Results

Sensitive strains of Staphylococcus are inhibited by concentrations of gentamicin of less than 1 mg/L4. Samples taken before splitting of the cement generally...
contained low concentrations of gentamicin with the exception of one specimen of joint fluid. After disruption of the cement, the concentration of gentamicin in tissue and fluid was considerably above active levels (Figs 1 to 5; Table I).

Discussion

The diagnosis of deep infection in a prosthesis is often challenging. Colonisation may be present with no clinical or mechanical manifestations. Laboratory investigations may be required including aerobic and anaerobic culture of material obtained at operation. In cases of two-stage revision for suspected infection it has been suggested that several different samples should be taken at the initial procedure. These specimens should be removed with different instruments and sent for analysis separately. Histological examination is also recommended to confirm the typical features of infection. An antibiotic in high concentrations in the operative field is likely to influence the microbiological analysis. Cultures should ideally isolate the same organism in three out of five specimens. Any organisms colonising the primary prosthesis, but not identified and eradicated, would be likely to infect the new implant and put the revised operation at risk of failure.
One of the implications of using cement containing gentamicin at primary hip replacement is the development of gentamicin-resistant organisms. Such antibiotic resistance may affect certain strains of coagulase-negative Staphylococcus but not others and this may give rise to diagnostic difficulties when multiple strains are a cause of infection; 30% of infections are reported to be due to this type of organism.²

Studies on infection after total hip replacement have suggested rates of infection of up to about 1.5% in operations in which no prophylactic systemic antibiotics had been used.⁵ Staphylococcus epidermidis and Staphylococcus aureus are the organisms most commonly isolated.⁶

Table I. Details of the five patients and of gentamicin concentrations in tissue samples before and after cement damage

<table>
<thead>
<tr>
<th>Cases</th>
<th>Age in years</th>
<th>Gender</th>
<th>Time of replacement in years after primary operation</th>
<th>Cement brand</th>
<th>Side</th>
<th>Gentamicin concentration before revision</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>Joint fluid (mg/l)</td>
</tr>
<tr>
<td></td>
<td>82</td>
<td>30</td>
<td>61</td>
<td>63</td>
<td>66</td>
<td>92.3 &lt;0.3 &lt;0.3 &lt;0.3 &lt;0.3</td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>6</td>
<td>2</td>
<td>8</td>
<td>10</td>
<td>468 80 328.5 93.3 30</td>
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<td></td>
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<td>12700</td>
<td>8140</td>
<td>3220</td>
<td>9108 8700 12700 8140 3220</td>
</tr>
</tbody>
</table>

Fig. 4
Gentamicin concentration in samples of bone cement taken from the five patients.

Fig. 5
Decreasing concentrations of gentamicin in bone cement with increasing time after insertion in the five patients (1 to 5).
ococcus aureus are isolated from 47% of infected total joint replacements, and Gram-negative organisms, including Pseudomonas, from 17%.6 Gentamicin is rapidly bactericidal for these organisms at concentrations above the minimum inhibitory concentration in non-resistant strains.

Our study has shown that if cement containing gentamicin has been used at the time of primary hip replacement, concentrations of antibiotic may still be extremely high in the cement many years later. After fracture of the cement at revision, gentamicin may be present in the tissues in very high concentrations which far exceed those required to kill the organisms that are responsible for most infections. This implies that accurate microbiological assessment of tissue removed after cracking of the cement may not be possible, since potential pathogens present in the joint may have been eradicated by the gentamicin. Few studies assessing infection after total hip replacement have taken full account of this, and only one has tackled the issue of gentamicin resistance and multiple strains of pathogen. Certainly, if more than one strain or pathogen is involved, only one may be isolated if gentamicin resistance has developed.

In one of our patients the gentamicin concentration in the joint fluid sampled before the cement had been cracked was very high (92.3 mg/l). Preoperative radiographs showed cement fragmentation, possibly causing antibiotic release in the weeks before revision surgery. This suggests that the diagnosis of infection by analysis of joint aspirates may lead to misleading results if gentamicin has been released into the fluid around a loose stem. In another of our patients, samples of joint capsule and membrane taken before disruption of cement contained concentrations slightly exceeding the minimum inhibitory concentration for staphylococci. Clinicians should be aware that antibiotic can be present in samples taken at any stage of a revision procedure.

Our study indicates that samples taken for microbiological analysis during revision hip arthroplasty which involves removal of cement containing gentamicin can be contaminated with antibiotic. We believe that the samples should be removed before the cement is disturbed and the laboratory warned of possible antibiotic contamination in all cases when cement containing gentamicin is being removed.

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References