Fluconazole-impregnated beads in the management of fungal infection of prosthetic joints

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We report two cases of fungal infection of prosthetic joints which were successfully treated by the incorporation of fluconazole into polymethylmethacrylate beads inserted at the time of debridement.

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To our knowledge, only 25 cases of fungal infection around prostheses have been reported.¹⁻¹⁸ There seems to be general agreement about the need for excision arthroplasty and prolonged intravenous administration of antifungal agents, usually amphotericin B. Staged reimplantation was attempted in six patients and was successful in four.^{2,3,12-14} Even-tual mycological cure may have been achieved, although the follow-up was less than a year in half of the cases. We incorporated fluconazole into polymethylmethacrylate (PMMA) in the form of beads as part of a two-stage surgical procedure in two patients. Infection of the joint by *Candida* was successfully eradicated in both.

Case reports

Case 1. A 51-year-old woman who had had a right total hip replacement in 1984 presented with hip pain in 1987. A biopsy, in 1990, revealed infection with *Candida parapsilosis*. In August 1991, a first-stage exchange procedure was undertaken with removal of all foreign material and infected tissue. *Candida parapsilosis* was again grown from the specimens. Methylmethacrylate beads were prepared by adding 2 g of fluconazole powder to one mix of Palacos R bone cement (Schering Plough Ltd, Mildenhall, UK), and made into chains. These were inserted into the acetabulum and femoral shaft before the wound was closed

over deep and superficial drains. Four days later treatment with oral fluconazole (200 mg twice daily) was started. The levels of fluconazole were measured in the fluid in the drain for six days after operation (Fig. 1). Specimens of tissue taken in February 1992, when the beads were removed, were sterile. In June 1992, a prosthesis was reimplanted with fluconazole again added to the cement. Specimens of tissue again did not grow any organisms. Oral fluconazole was not administered. There has been no evidence of recurrence of infection for seven years.

Case 2. A 68-year-old woman underwent a replacement of the femoral head for a subcapital hip fracture in 1994. In 1996, the implant was clinically and radiologically loose. Aspirate from the hip grew *Candida albicans*. First-stage exchange surgery was carried out as described above and infection with *Candida albicans* confirmed. Again 2 g of fluconazole were placed in 'home-made' Palacos R beads, and oral fluconazole was administered by the same regime. The levels of fluconazole measured from the deep and superficial drains are shown in Figure 2. Reimplantation was undertaken three months later without an intervening biopsy or administration of systemic fluconazole. Tissue specimens were sterile. The patient died more than four years later with no sign of recurrence of the infection, either clinically or radiologically.

Fig. 1

Case 1. The fluconazole concentration in the fluid from the deep and superficial drains (arrow indicates the commencement of oral fluconazole).

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Fig. 2

Case 2. The fluconazole concentration in the fluid from the deep and superficial drains (arrow indicates the commencement of oral fluconazole).

Discussion

In the management of fungal infection around prostheses it has been stated that removal of the prosthesis and prolonged administration of amphotericin B are essential in order to eradicate the infection.^{13,19} An antifungal drug which remains effective after incorporation into PMMA bone cement may be a useful alternative.¹⁹

Many heat-stable antibiotics elute from PMMA cement in a predictable manner and Palacos cement has elution characteristics which seem particularly favourable.^{20,21} The addition of many antibiotics in a dose adequate enough to give high local levels with very low systemic levels, does not seem to have a significant effect on the mechanical properties of cement. Preliminary studies on the in vitro elution of fluconazole from Palacos R at our hospital confirmed that detectable fungicidal levels could be obtained for several days. Figure 1 shows that the levels obtained in the deep tissues in our first patient (case 1) were very high. Oral fluconazole was prescribed after the first four days as a precautionary measure because the in vitro study had demonstrated a significant fall in concentration after this period. The levels in the superficial drain rose and were reasonably constant at about 5.5 mg/l. There was a different pattern in our second patient (Fig. 2). Very high levels were obtained initially and were maintained at approximately 5 mg/l for several days. The level in the superficial drain was low and was not raised significantly by the oral administration of fluconazole after four days. The total amount of fluconazole eluted was 21 mg in case 1 and 13.9 mg in case 2. The volume of drainage in the second patient was significantly higher than in the first (4.1 l v 1.0 l), but this does suggest that predictably high levels around the joint cannot be guaranteed with orally

administered fluconazole. The high local levels obtained from impregnated PMMA seem to be predictable and reliable, and oral supplementation may not be required, as has been our experience with pyogenic deep sepsis.

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