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TECHNICAL NOTE

Practical considerations in the making and use of high-dose antibiotic-loaded bone cement

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Local antibiotic delivery with antibiotic loaded acrylic bone cement has been used extensively in the management of chronic osteomyelitis and implant related infections. Though newer drug delivery vehicles are being investigated, it remains the most widely used local antibiotic delivery vehicle in orthopaedic surgery. Self- made antibiotic loaded bone cement beads, which are cheaper and antibiotic specific, have been shown to elute less effectively than commercial antibiotic loaded cement beads. We offer several tips for increasing the elution and effectiveness of antibiotic loaded bone cement in clinical practice.

Keywords : antibiotic bone cement ; beads ; preparation ; antibiotic elution.

INTRODUCTION

Since its introduction in 1970 by Buchholz and Engelbrecht, antibiotic-loaded acrylic bone cement has been used extensively in the treatment of orthopaedic infections (*2*). It remains the current gold standard for local antibiotic delivery in orthopaedic surgery as it is a proven way to deliver high concentrations of the drug locally, especially to poorly vascularized tissues (*1,2,5,6,12*). It also results in a lower serum antibiotic concentration than that associated with systemic administration, thereby reducing toxicity-related side effects (*2,6*). Self- made antibiotic loaded bone cement beads are cheaper, antibiotic specific and have no availability issues. However they have been shown to elute less effectively than commercial antibiotic loaded cement beads (*15*). We offer several tips for increasing the elution and effectiveness of antibiotic loaded bone cement in clinical practice and discuss the rationale behind them.

TECHNIQUE

The liquid monomer is added to methylmethacrylate powder in an inert bowl with a spatula as per the manufacturer's instructions, and hand mixing is commenced. At the early 'dough' phase, immediately after wetting the cement, the antibiotic powder of appropriate weight for the desired formulation is added and thoroughly mixed with the cement mixture in a standard fashion of one revolution per second to obtain a homogeneous compound. The choice of the antibiotic is determined by

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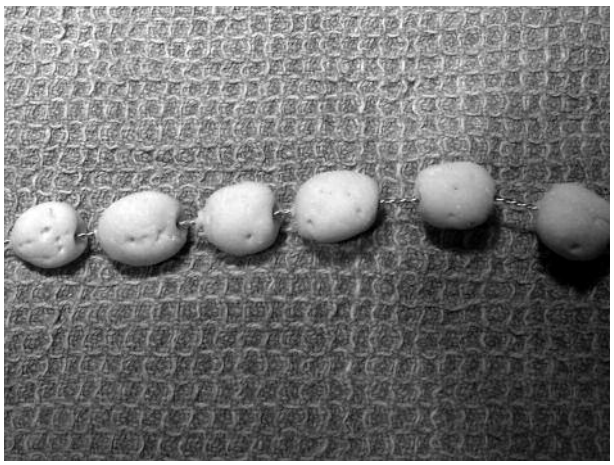

Fig. 1. — Self made antibiotic loaded bone cement beads strung on a braided stainless steel wire.

pre-operative culture report if present. Two antibiotics are chosen in the presence of mixed infections. When pre-operative culture reports are unavailable, it is desirable to provide broad spectrum Gram-positive and negative coverage with two antibiotics. We use 2 gm each of meropenem and vancomycin for a 40 gm batch of bone cement in such situations (total antibiotic concentration : 10%).

Prior to the mixing of the antibiotic bone cement, two to three strings of braided stainless steel wires are made. These are made by holding a pair of 22 or 24 gauge stainless steel wires with a clamp in one end and a vise in the other end and twisting them in order to braid them. The cement beads are made as small as possible (about 8 mm) and strung on to the braided stainless steel wires. It is essential to ensure that adjacent beads have a free gap between each other and are not in contact. A further attempt to increase the surface area is made by making multiple pits on the surface of the cement beads using a 1.5 mm Kirschner wire as it starts to set (fig 1).

After setting, the antibiotic beads are placed *in vivo*. It is desirable to not only be in as close proximity as possible to the focus of infection but to also span it. The wound is closed meticulously in layers over a suction drain. This suction drain is however kept closed. The drain is opened every 6 to 8 hours for only 15 minutes to allow periodic drainage of the wound.

DISCUSSION

Sensitivity of bacteria is currently reported on the basis of achievable serum levels of the antibiotic when systemically administered. Most bacteria defined as resistant by these criteria might be sensitive to the same antibiotic when exposed to high local tissue levels as achievable by antibiotic loaded bone cement (*6*). Successful therapy would therefore depend on achieving high local antibiotic concentrations. Hanssen classified antibiotic loaded bone cement into high dose (> 2 g antibiotic per 40 g of cement) and low dose (< 2 g antibiotic per 40 g of cement) and recommended high dose for use as beads or spacers and low dose for prosthesis fixation (*7*). It is postulated that mixing high doses of powdered antibiotics considerably increases cement porosity and facilitates increased elution of antibiotics (*9,11*). The usual method advocated for making antibiotic loaded bone cement is mixing the antibiotic powder to the cement powder after which the liquid monomer is added. High volumes of the antibiotic powder make mixing difficult by this method as much of the liquid monomer is lost in dissolving the antibiotic powder. Instead one could first mix the polymethylmethacrylate monomer and cement powder together to form the liquid cement to which the antibiotic powder is added.

The elution of antibiotics occurs from the surface of the bone cement and also from the pores and cracks in its matrix (*9,10*). Elution is improved with increasing surface area and porosity of the cement exposed to liquid medium (*9-11*). We would like to make two observations in this regard. Firstly, given the time consideration, we find that it is difficult to make symmetrical spheres as advised and the beads end up being more oval. It is more important to ensure that the beads are kept small in size and the beads are so strung on the stainless steel wire that there is a gap between adjacent beads (*10,15*). The use of Kirschner wires to make multiple pits on the surface of the beads to increase the surface area aids better elution of the antibiotic. Secondly, the porosity of bone cements depends on the viscosity of the cement, higher viscosity cements possessing a higher porosity than low viscosity ones (*14*). We currently use high viscosity CMW1 bone cement to

make antibiotic beads. The added advantage of using high-viscosity cement is that it gives a long working time to make the beads.

The addition of two antibiotics to acrylic bone cement has been shown to increase the elution of the antibiotics possibly by increasing its porosity (*1,2,5,8,13*). Studies have shown that the addition of meropenem increases the elution of vancomycin (*1*). This phenomenon has been reported previously for other combinations of vancomycin with another antibiotic and is referred to as passive opportunism (*2,5,8,13*). The second positive effect of dual antibiotic loaded bone cement is the broadening of the antibacterial spectrum (*1,2,8*).

Antibiotic loaded acrylic bone cement delivers antibiotics locally but there is not much literature to reveal how far from the beads effective antibiotic levels will be maintained. Though this would depend on the local milieu, it has been suggested that it is no more than 2-3 cm (*3*). Hence it would seem rational to assume that it is essential to be in as close proximity as possible to the focus of infection and also to span it.

The antibiotic is leached from the cement beads into the postoperative wound haematoma which acts as a transport medium. The placement of a drain would lead to the removal of collected haematoma and with it the eluted antibiotic and is hence not recommended (*4*). Practical considerations however necessitate a drain after debridement. Our method allows the collected haematoma with the eluted antibiotic to act locally before being drained out periodically. Drain removal is done when the drainage level decreases in 48-72 hours as usual.

Removal of antibiotic loaded bone cement after control of infection is desirable. However removal of these beads may be difficult because they are encased in dense fibrous tissue. Many a times, during bead removal, traction is exerted on the stainless steel wires. The use of braided stainless steel wires provides a better hold on the beads when compared to a single smooth stainless steel wire and decreases the chance of the beads from slipping out of the stainless steel wire.

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