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Release of gentamicin from bone cement

An ex-vivo study

Gentamycin-loaded cement from 16 patients undergoing revision of hip arthroplasty was studied. Samples removed at surgery were analyzed for gentamicin using an enzyme-linked immunoassay. Seventy-eight (55–98) per cent of the gentamicin was retained within the cement after 24 (1–48) months.

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Use of acrylic cement containing gentamicin, has reduced the infection rate in total hip arthroplasty (Buchholz & Gartman 1972).

The amount of antibiotic released declines sharply after the initial peak levels. In a detailed clinical study, Törholm et al. (1983) have accounted for 5–18 per cent of the gentamicin included in the cement. They postulated that a further 5–10 per cent is lost in wound secretions, thus leaving between 75 and 80 per cent of the antibiotic unaccounted for. They suggested that the cement "continues to release gentamicin in vivo for long periods."

We have measured the amount of gentamicin left within the acrylic cement after various periods of time during which the cement has remained in the body.

Material and methods

Sixteen patients requiring revision of hip arthroplasties and known to have had acrylic cement with gentamicin (Palacos^{R}) were included in the study. The indications for re-operation were deep sepsis, loose prosthesis, fracture, and dislocation. The mean duration from the primary operation to removal of cement was 24 (1–48) months. The removed cement was used for gentamicin level estimations.

Extraction of gentamicin

Samples of cement chippings (approx. 0.5 g) were accurately weighed into volumetric flasks fitted with airtight stoppers. 20 ml of chloroform was added and the flasks were agitated intermittently for several hours. They were left overnight at room temperature to allow the polymer to dissolve and to release chloroform-insoluble gentamicin. 20 ml of phosphate-buffered saline (pH 7.5) was then added to each flask and after mixing and standing overnight, the aqueous layer was separated by centrifuging and collected as the extract. This extract was assayed by enzyme-linked immunoassay using the EMIT system from SYVA Ltd. In order to use the EMIT assay, a full calibration curve was prepared in accordance with the manufacturer's protocol. The extracts were assayed at a dilution of 1 in 20 using phosphate-buffered saline as the dilutent. The calibration data was analyzed by computer using a nonlinear least square algorithm based on a five-parameter logit function.

The concentration of gentamicin in each extract was calculated from the calibration curve, and from this result the amount of gentamicin in the original sample was calculated using the formula

$$Pc = \frac{Ec \times D \times V}{W \times 1000}$$

$$Pc = \frac{mg/ml \times D \times ml}{g \times 1000} = \frac{mg \times D}{g \times 1000} = \frac{mg \times D}{g}$$

Pc = gentamicin in Palacos $^{(R)}$ sample in mg/g
Ec = gentamicin in extract in mg/ml

D = Dilution factor = 20
V = Extraction factor = 20
W = Weight of sample in g

Results

The results showed a mean concentration in the removed cement of 5.94 (4.19–6.78) mg/g.

Two controls were used – one at the beginning, the other in the middle of the estimations. Both gave identical results: 7.5 mg/g of cement.

Discussion

When analyzing the results of this study, certain possible sources of error must be considered.

The total weight of each pack, excluding gentamicin, is 58.8 g. With the gentamicin content ranging from 0.475 to 0.575 g (personal communication from suppliers), the expected range of values would be 8.0 to 9.7 mg of gentamicin per gram of the antibiotic-cement mixture.

Assuming that the mean assay value for the control indicated the percentage extractable quantity, as indicated in the original mix, then the method presented in this study allowed an extraction of between 94 and 78 per cent. This calculation does not take into account any change in weight resulting from polymerization. Thus, the method of gentamicin extraction allows only ranges to be taken into consideration, rather than absolute values of the antibiotic. Any sample containing fragments of bone or dried blood will affect the exact weight of the cement. Further, any such sample may not be representative of the cement as a whole, and any possible differences between the femoral and the acetabular cement were not taken into account. We consider, however, that comparison of the results between the samples tested was reasonably accurate to allow the following conclusions to be drawn.

On an average, 78 (55–98) per cent of the gentamicin was retained within the acrylic cement. Thus, the amount of gentamicin released was, on an average, 2 (0.1–3.4) mg per gram of polymerized cement.

During the period under study, 1–48 months after the primary hip operation, we did not find any substantial loss of gentamicin from the cement.

The findings of the study do not detract from the efficacy of the antibiotic-loaded acrylic cement as a method of preventing or treating infection. What they do show, however, is that it cannot be relied upon to release all the antibiotic over a prolonged period of time. Therefore, it does not protect against late hematogenous infection.

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