Liquid gentamicin and vancomycin in bone cement: a potentially more cost-effective regimen

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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

CRD summary
This study evaluated the effectiveness and costs of liquid gentamicin alone or with powdered vancomycin, in antibiotic impregnated poly(methyl methacrylate) bone cement. The authors concluded that combining gentamicin and vancomycin was cost-effective, but was limited to temporary use for active infections. Further study in patients, rather than a laboratory, was necessary. The study was thorough and clearly reported, with transparent methods, but was limited by the setting and exclusion of a relevant comparator. Research should address these limitations.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
This study evaluated the effectiveness and costs of liquid gentamicin alone or with powdered vancomycin, in antibiotic impregnated poly(methyl methacrylate) bone cement.

Interventions
Three antibiotic regimens were mixed with the bone cement. One was 480mg of liquid gentamicin sulphate added to 20mL of a liquid monomer; the second was 4g of vancomycin hydrochloride powder; and the third was a combination of the first two regimens. All three options were compared with the bone cement without antibiotics, as a control for its mechanical properties.

Location/setting
Taiwan/hospital laboratory.

Methods
Analytical approach:
The material properties and antibiotic effectiveness were from a study that investigated them in vitro, over five weeks. The study perspective was not explicitly stated.

Effectiveness data:
The effectiveness data were from in vitro laboratory testing. The primary measures of effectiveness were antibiotic elution, antibiotic effectiveness, sample cross-sectional porosity, and compressive strength. Antibiotic elution was determined by measuring its concentration by fluorescence polarisation immunoassay. Antibiotic effectiveness against methicillin-resistant Staphylococcus aureus (MRSA) and Pseudomonas aeruginosa (P. aeruginosa) was measured by bactericidal activity (1,000-fold decrease in the number of viable bacteria within eight hours of incubation). Porosity distribution, as a percentage of cross-sectional area, was evaluated using a reflected-light microscope and image analysis. Specimens were tested for axial compression, using a specially designed machine that compressed each specimen at 0.1mm per second, and measured force, displacement, and time simultaneously.

Monetary benefit and utility valuations:
Not relevant.

Measure of benefit:
There was no summary measure of benefit. The outcomes were antibiotic elution, antibiotic effectiveness, sample cross-
sectional porosity, and compressive strength.

Cost data:
The acquisition costs for the drugs were from the Chang Gung Memorial Hospital in Taiwan. They were reported in US $.

Analysis of uncertainty:
The differences between intervention results were compared for statistical significance.

Results
Over the five weeks, the combination of gentamicin and vancomycin increased drug elution; vancomycin elution was increased by 146% (p<0.01) and gentamicin elution was increased by 45% (p<0.01), compared with each drug alone. After eight hours, vancomycin alone was bactericidal for MRSA, but ineffective against *P. aeruginosa*. Gentamicin was bactericidal for *P. aeruginosa*, but ineffective against MRSA. Together, they were bactericidal after four hours for MRSA, and eight hours for *P. aeruginosa*.

Porosity in the specimens was increased compared with control (p<0.001), except for vancomycin alone, which was not statistically significant (p>0.05). Porosity was 5.8% (SD 2.6) for vancomycin alone, 16.8% (SD 1.9) for gentamicin alone, 22.4% (SD 3.4) for the combination, and 4.2% (SD 2.1) for the control group.

Ultimate compressive strength was reduced, by 13% for vancomycin alone, by 37% for gentamicin alone, and by 45% for the combination. The authors indicated that, in the temporary treatment of active infection, a decrease in ultimate compressive strength of 45% was not a problem.

The costs for liquid gentamicin were estimated to be $4 for a 480mg dose. The cost of tobramycin powder 1.2g (used in combination with vancomycin, but in limited supply) was $120 per dose.

Authors' conclusions
The authors concluded that combining gentamicin and vancomycin in bone cement was cost-effective, but was limited to temporary use for active infections. Further study of efficacy and safety, in patients rather than in vitro, was necessary.

CRD commentary
Interventions:
The interventions were thoroughly described and appear to have been appropriate, but a relevant comparator, tobramycin, was not included. The justification for studying liquid gentamicin was that powdered tobramycin was too expensive (powdered gentamicin was equally expensive). The costs were reported only for gentamicin and tobramycin; tobramycin should have been evaluated for effectiveness.

Effectiveness/benefits:
The effectiveness data and methods were clearly reported. The effectiveness and benefits were based on in vitro results, a limitation which the authors acknowledged; they indicated that further in vivo analysis was necessary and that a study was in progress.

Costs:
The costs were presented from the perspective of the Chang Gung Memorial Hospital. They only included gentamicin and tobramycin drug costs; vancomycin costs were not reported, and tobramycin was not analysed. As the costs were limited to the drugs and the setting was a laboratory, potential health care costs could not be analysed. The price year was not reported, so attempts to transfer and inflate the costs for other settings will be difficult. The costs were from one hospital in Taiwan, which may not be generalisable to other settings.

Analysis and results:
The results were well reported, but the nature of the study limits their applicability to clinical practice. The authors thoroughly discussed the limitations of their study, acknowledging the need for in vivo studies and the insufficiency of
the in vitro evidence for clinical practice, and acknowledging that only one bone cement method was used, while in practice many techniques are used with differences in effectiveness and mechanical properties. They compared these results with those of other studies, which included tobramycin, but as the different mixture methods produced different results, analysing tobramycin alone and with vancomycin, in this study, would have been appropriate.

Concluding remarks:
The study was thorough and clearly reported, with transparent methods, but was limited by the in vitro testing, and lack of comparison with tobramycin for effectiveness. Future research should address these limitations.

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