Linezolid – impregnated acrylic bone cement – a new therapeutic option

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Introduction

Bacterial adherence to and persistence on antibiotic-loaded bone cement is an increasing problem. New antibiotics with good antimicrobial and pharmacokinetic properties (e.g. linezolid) may be the solution to this problem; however, few data concerning linezolid-loaded acrylic cement are currently available.

Materials - Methods

Initially, a preliminary test series with various linezolid concentrations was carried out in order to determine the ideal antibiotic amount for PMMA impregnation with regard to elution and antimicrobial properties. Four different combinations (1.2 g linezolid/80 g PMMA, 2.4 g linezolid/80 g PMMA, 1.2 g linezolid/1 g gentamicin/80 g PMMA, 2.4 g linezolid/1 g gentamicin/80 g PMMA) were tested. All combinations were tested twice. Gentamicin-linezolid-loaded spacers were tested in order to determine a possible synergistic effect between these two antimicrobial groups. The chosen concentrations for linezolid were 1.2 g (single daily dose) and 2.4 g / 80 g PMMA (double daily dose). The cement used was Palacos and Refobacin-Palacos R (1 g gentamicin/80 g PMMA). The results of the preliminary test series showed that the best combination tested with regard to antibiotic elution and antimicrobial properties was the one consisting of gentamicin and 2.4 g linezolid.

For the actual test series, ten gentamicin-linezolid-loaded hip spacers (1 g gentamicin/2.4 g linezolid/80 g PMMA; five spacers including a metallic endoskeleton, five with no metallic components) were tested in vitro against a strain of methicillin-resistant Staphylococcus aureus (MRSA) with regard to antibiotic release and bacteria growth inhibition. Daily, the antibiotic elution was determined by high liquid performance chromatography (linezolid) and fluorescence polarization immunoassay (gentamicin), the bacteria growth inhibition photometrically at 546 nm.

Statistical analysis was carried out with the SPSS 12.0 program.

Results

Both antibiotics demonstrated similar elution kinetics. Peak average concentrations were reached on day 1 (35.10 µg/mL gentamicin [24.10-52.52], 36.28 µg/mL linezolid [22.87-71.76]). Highest gentamicin values were reached at 52.52 µg/mL from a spacer containing a metallic endoskeleton, whereas highest linezolid concentrations were reached at 71.76 µg/mL from a spacer containing no metallic components.

After 8 days in vitro, 0.97 % [0.93 – 1.05 %] of the initial amount of linezolid and 3.13 % [2.85 – 3.31 %] of gentamicin were meanly released from spacers containing a metallic endoskeleton. In those containing of simple cement these values were 1.22 % [0.91 – 1.59 %] and 2.67 [2.12 – 2.73 %], respectively.

Discussion

Linezolid demonstrated acceptable elution kinetics from bone cement, however, further experimental research and animal studies should clarify any possible side effect of linezolid-loaded cement media before definitive use in the clinical practise. Moreover, future studies should investigate whether the insertion of a metallic endoskeleton has a similar effect on the elution properties of other antimicrobial agents, because if so, its use in clinical practise in the treatment of hip joint infections should be questioned.