Rev Esp Cir Ortop Traumatol. 2018;62(1):86–92

Revista Española de Cirugía Ortopédica y Traumatología

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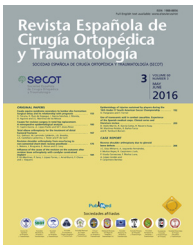

RESEARCH

New method for antibiotic release from bone cement (polymethylmethacrylate): Redefining boundaries☆

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Received 1 March 2017; accepted 30 August 2017

KEYWORDS
Rifampicin;
Polymethylmethacrylate;
Microcapsules;
Cement spacers;
Periprosthetic infection

Abstract
Introduction: The increasing antimicrobial resistance is promoting the addition of antibiotics with high antistaphylococcal activity to polymethylmethacrylate (PMMA), for use in cement spacers in periprosthetic joint infection. Linezolid and levofloxacin have already been used in in vitro studies, however, rifampicin has been shown to have a deleterious effect on the mechanical properties of PMMA, because it inhibits PMMA polymerisation. The objective of our study was to isolate the rifampicin during the polymerisation process using microencapsulation techniques, in order to obtain a PMMA suitable for manufacturing bone cement spacers.
Material and method: Microcapsules of rifampicin were synthesised with alginate and PHBV, using Rifaldin®. The concentration levels of rifampicin were studied by UV–vis spectrophotometry. Compression, hardness and setting time tests were performed with CMW®1 cement samples alone, with non-encapsulated rifampicin and with alginate or PHBV microcapsules.
Results: The production yield, efficiency and microencapsulation yield were greater with alginate ($p = 0.0001$). The cement with microcapsules demonstrated greater resistance to compression than the cement with rifampicin (91.26 ± 5.13, 91.35 ± 6.29 and 74.04 ± 3.57 MPa in alginate, PHBV and rifampicin, respectively) ($p = 0.0001$). The setting time reduced, and the hardness curve of the cement with alginate microcapsules was similar to that of the control.

☆ Please cite this article as: Carbó-Laso E, Sanz-Ruiz P, del Real-Romero JC, Ballesteros-Iglesias Y, Paz-Jiménez E, Arán-Ais F, et al. Nuevo método de liberación de antibióticos del cemento óseo (polimetilmetacrilato): redefiniendo los límites. Rev Esp Cir Ortop Traumatol. 2018;62:86–92.

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Discussion and conclusions: Microencapsulation with alginate is an appropriate technique for introducing rifampicin into PMMA, preserving compression properties and setting time. This could allow intraoperative manufacturing of bone cement spacers that release rifampicin for the treatment of periprosthetic joint infection.

PALABRAS CLAVE
Rifampicina;
Polimetilmetacrilato;
Microcápsulas;
Espaciadores de cemento;
Infección periprotésica

Nuevo método de liberación de antibióticos del cemento óseo (polimetilmetacrilato): redefiniendo los límites

Resumen
Introducción: La creciente resistencia a antimicrobianos está impulsando la adición de antibióticos con elevada actividad antiestafilocócica al polimetilmetacrilato (PMMA), para su uso en los espaciadores de cemento en la infección periprotésica. El linezolid o el levofloxacino ya han sido utilizados en estudios in vitro; sin embargo, la rifampicina ha demostrado un efecto deletéreo sobre las propiedades mecánicas del PMMA, inhibiendo su polimerización. El objetivo de nuestro estudio fue aislar la rifampicina durante el proceso de polimerización mediante técnicas de microencapsulación, con el fin de obtener un PMMA apto para la fabricación de espaciadores articulares.
Material y método: Se sintetizaron microcápsulas de rifampicina con alginato y PHBV, utilizando Rifaldin®. Se estudió la concentración de rifampicina mediante espectrofotometría UV-visible. Se realizaron ensayos de compresión, dureza y tiempo de fraguado con probetas de cemento CMW® 1 solo, con rifampicina y microcápsulas de PHBV y alginato.
Resultados: El rendimiento de producción, la eficiencia y el rendimiento de microencapsulación fueron mayores con alginato (p = 0,0001). El cemento con microcápsulas mostró mayor resistencia a la compresión que el cemento con rifampicina (91,26 ± 5,13, 91,35 ± 6,29 y 74,04 ± 3,57 MPa en alginato, PHBV y rifampicina, respectivamente) (p = 0,0001). El tiempo de fraguado disminuyó, siendo la curva de dureza del cemento con microcápsulas de alginato similar a la de control.
Discusión y conclusiones: La microencapsulación con alginato es una técnica adecuada para introducir rifampicina en el PMMA preservando las propiedades de compresión y el tiempo de fraguado. Su obtención permitiría fabricar espaciadores que liberasen localmente rifampicina para el tratamiento de la infección periprotésica.

Introduction

Periprosthetic joint infection is a serious complication, the prevalence of which has risen in the last few decades. It has been estimated that this will be the most common cause of prosthetic revision surgery in the next 2 or 3 decades.[1,2] The appearance of multi-resistant germs and the medical complexity of patients have imposed modification of existing surgical protocols which are insufficient for optimum management of such a complex problem, in addition to investigating new forms of treatment.

The majority of microorganisms which cause periprosthetic infection are producers of biofilm. The bacteria inside the biofilm radically change their phenotype leading to bacterial growth with a metabolically low activity and enabling bacteria to survive during chronic infection.[3] This means that in conditions of mature biofilm, the active in vitro doses of the antibiotic are 200–1000 times higher than the standard dosis,[4] making it impossible to treat periprosthetic infections with antibiotics alone, administered systemically. Elevated concentrations of antibiotic on the infection site raises the probability of success of the treatment and this may be achieved through the use of antibiotic-impregnated cement spacers.

The two-stage exchange arthroplasty is considered to be the gold standard treatment for chronic periprosthetic infection. After the removal of the joint prosthesis and debridement of infected tissues, a bone cement spacer is temporally inserted with a high dose of antibiotics aimed at preserving the joint space and achieving high local levels of antibiotics. Amino glucosides and vancomycin are the most commonly used antibiotics added to the bone cement, but the appearance of multi-resistant strains of bacteria is threatening their efficacy in local treatment.[5]

The role of rifampicin against staphylococcal infections associated with implants has been demonstrated.[6] Rifampicin, in combination with other antibiotics is considered to be the antibiotic of choice in the treatment