Efficacy of colistin-loaded cement spacer in carbapenem-resistant *Klebsiella pneumoniae* experimental prosthetic joint infection

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ABSTRACT

BACKGROUND: In a new rabbit model of carbapenem-resistant *Klebsiella pneumoniae* knee-prosthesis infection, we studied the efficacy of colistin cement alone or in combination with systemic intramuscular (i.m.) injections of colistin.

METHODS: Seven days after infection, surgical debridement and removal of the infected prostheses were performed, and rabbits were randomly assigned to one of four different treatment groups of twelve rabbits: prosthesis replacement by drug-free cement spacer (control) prosthesis replacement by colistin-loaded cement spacer (3 MUI of colistin/40 g of cement) (colistin local) , prosthesis replacement by drug-free cement spacer and i.m. colistin (12 mg/kg of body weight, three time a day for 7 days), or colistin local + i.m.

RESULTS: We observed a statistically significant difference (p = 0.049) between the colistin local + systemic group and the control group in the criteria of number of rabbits with sterile bone under the total number of rabbits.

INTRODUCTION

Prosthetic joint infections (PJI) entails major morbidity and high costs. Carbapenem-resistant *Klebsiella pneumoniae* (CRKP) are emerging multidrug-resistant bacteria responsible for a broad range of invasive infections, including PJI, with limited therapeutic options. Although experts recommend various treatment combinations, data from clinical studies are scarce, and innovative experimental models are warranted to evaluate new medical and surgical treatments.

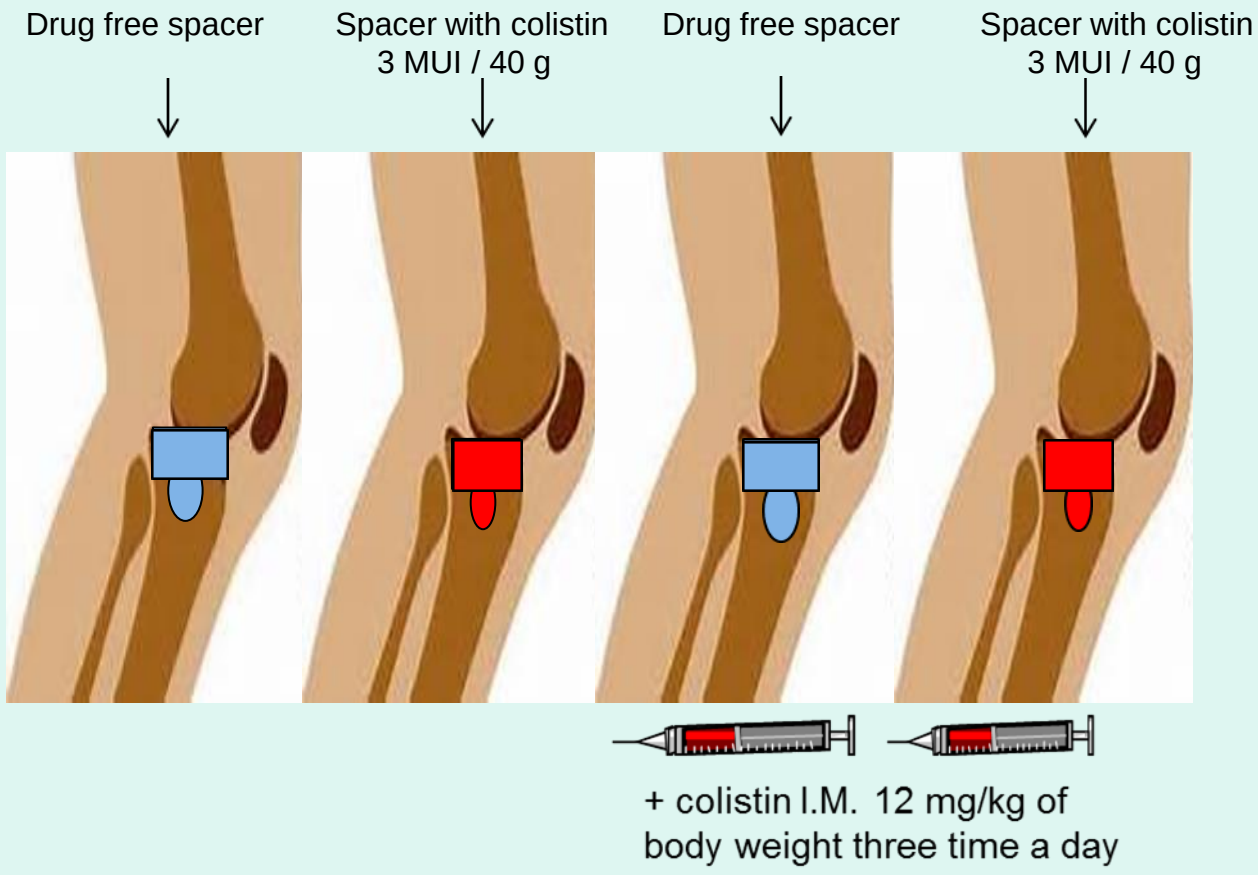
Colistin is often the only remaining option for treating CRKP. However, parenteral administration of colistin poses a high risk of adverse effects, including nephrotoxicity and neurotoxicity. Local administration is therefore a tempting approach to reduce the risk of side effects. Colistin elution from bone cement has been studied in vitro. Colistin-loaded bone cement also be used for the prevention of infection in total joint replacement.

STUDY OBJECTIVE

The aim of this study was to evaluate the efficacy of a colistin-impregnated cement spacer alone or combined with systemic colistin, using a new rabbit model of CRKP knee -prosthesis infection that closely mimics human infection, inspired by a previous model.

MATERIAL AND METHODS

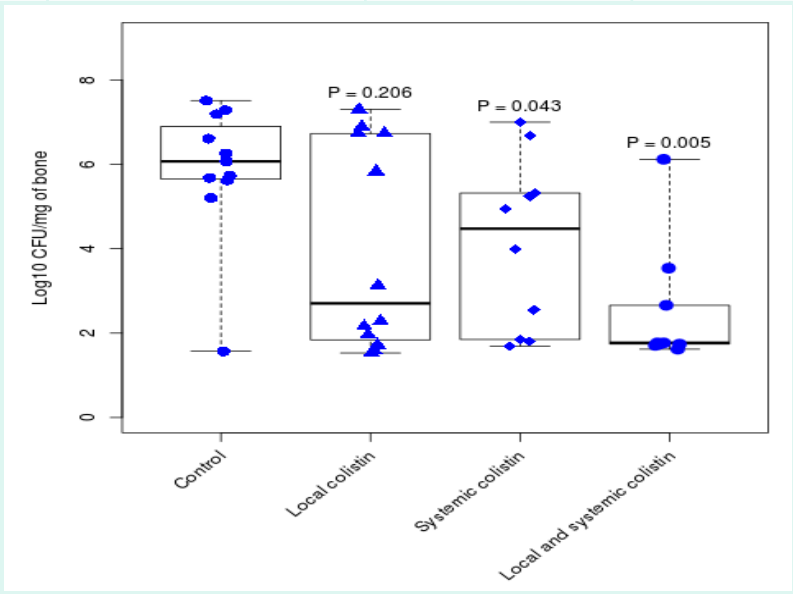
Different treatment groups seven days after prosthesis implantation and infection by 0.5 ml of 1.10^9 KPC 99 YC



RESULTS

Antibiotic efficacy against experimental carbapenem-resistant *Klebsiella pneumoniae* prosthetic knee infection model in rabbits

Treatment	No. of rabbits with sterile bone/total no. of rabbits	P versus control group (significant if <0.05)	log10 CFU/g of bone (mean ± SD)	P versus control group (significant if <0.05)
Control	0/10		5.9 ± 1.6	
Colistin local	3/12	0.590	4.0 ± 2.4	0.206
Colistin i.m.	3/10	0.311	4.1 ± 2.0	0.043
Colistin local + i.m.	5/9	0.049	2.5 ± 1.5	0.005



CONCLUSION

Combination of systemic and local colistin could be an interesting therapeutic option to cure carbapenem-resistant *Klebsiella pneumoniae* peri prosthetic joint infection.

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