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

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ABSTRACT

BACKGROUND

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

METHODS

Seven days after infection (day 7), surgical debridement and removal of the infected prostheses were performed, and rabbits were randomly assigned to different groups of 12 rabbits:
i) prosthesis replacement by drug-free cement spacer prosthesis (control)
ii) replacement by colistin-loaded cement spacer: 3 MUI of colistin/40 g of cement (colistin local)
iii) replacement by drug-free cement spacer and i.m. colistin, 12 mg/kg t.i.d. x 7 days (colistin i.m.)
iv) colistin local + i.m.
Rabbits were euthanized at day 14.

RESULTS

Only rabbits who received colistin local + i.m were more likely to have sterile bone, as compared to controls (56% vs. 9%, P=0.049). Rabbits who received colistin local + i.m. or colistin i.m. only had lower bacterial load as compared to controls (P=0.005, and 0.043, respectively)

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.**

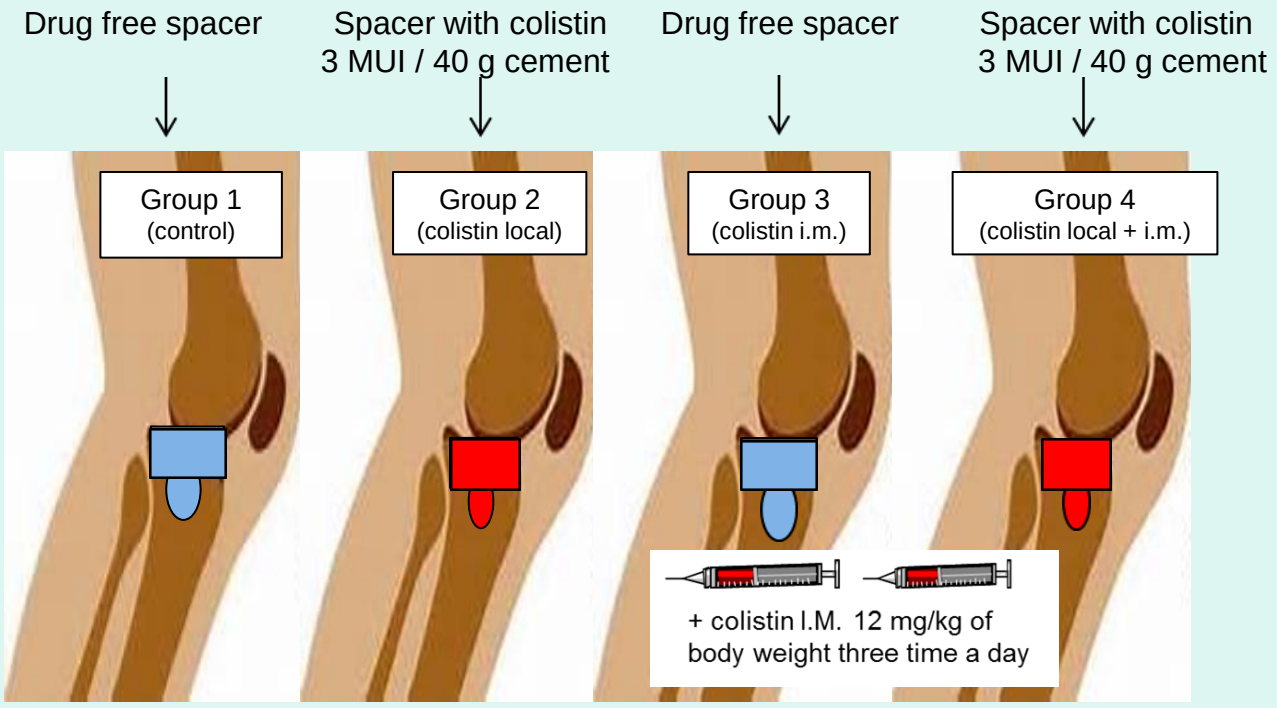
Colistin is often the last bullet for CRKP infections. However, parenteral administration of colistin poses a high risk of adverse effects, including nephrotoxicity and neurotoxicity. Local administration is therefore a tempting approach to reduce the risk of side effects. Colistin elution from bone cement has been evaluated *in vitro*.

STUDY OBJECTIVE

We aimed **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 mimics human infection, adapted from a previous model.

MATERIAL AND METHODS

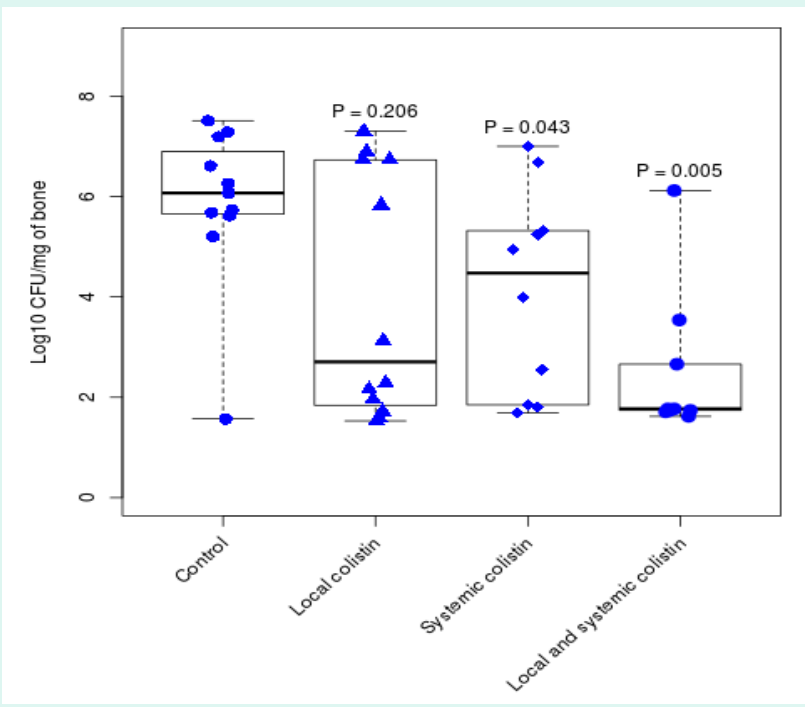
4 treatment groups 7 days after prosthesis implantation and infection by 0.5 ml of 1.10^9 KPC 99 YC



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	log10 CFU/g of bone (median [IQR])	P versus control group
Controls	**1/11**		**6.1 [5.7, 6.9]**	
Colistin local	3/12	0.590	4.5 [2, 5.3]	0.206
Colistin i.m.	3/10	0.311	**2.7 [1.9, 6.7]**	**0.043**
Colistin local + i.m.	**5/9**	**0.049**	**1.8 [1.7, 2.7]**	**0.005**



Whiskers represent minimum and maximum values; the horizontal line in each box plot, which cover the interquartile range, is the median. There were no differences between colistin local + I.M and colistin I.M alone on CFU and % of sterile bone (p= 0.051 and 0.37, respectively)

CONCLUSION

This innovative rabbit model of carbapenem-resistant *Klebsiella pneumoniae* prosthetic joint infection suggests that **the bactericidal effect of colistin is optimized through the combination of systemic and local administration.**

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