Antipseudomonal activity of free and nano-encapsulated tobramycin

Eva Armengol[1], Josep Mª Sierra[1], Héctor Rudilla[1], Rocío Herráez[1], Guadalupe Jiménez [1], Pablo Betancourt[1] , Teresa Vinuesa[1] and Miguel Viñas [1]

[1] *Laboratory of Molecular Microbiology and Antimicrobials. Dept. Pathology and Experimental Therapeutics. Universitat de Barcelona. eva.armengol.rivero@gmail.com*

Cystic fibrosis (CF) is a genetic disorder, leading to the the appearance of frequent pulmonary infections. One of the major pulmonary pathogens that colonize the respiratory tract of CF patients is *Pseudomonas aeruginosa* causing a chronic airway infection that persist over the course of time. The treatment to fight this pathogen is critical for the patient survival. Tobramycin is used to combat *P. aeruginosa,* but the emergence of tobramycin-resistant bacteria occurs frequently, the use of nanoparticles overcome this trouble[2]. Solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC) were designed for the treatment of *P. aeruginosa* infections in cystic fibrosis patients to reduce systemic toxicity, reduce the dose or administration intervals and look for alternative methods of antibiotic administration, such as aerosols[1]. To evaluate the antipseudomonal activity to free and nano-encapsulated tobramycin a total of 34 clinical isolates (Vall d'Hebron Hospital and Sant Joan de Déu Hospital) from cystic fibrosis patients were used. The drug susceptibility was determined by using broth microdilution method. Minimal biofilm eradication concentration (MBEC) was used to determine the efficacy of formulations of tobramycin against biofilms. The MBEC was established where no visible growth of bacteria was present after 24h incubation at 37 °C. Time-kill curves were also performed to assess the bactericidal activity of free and nanoencapsulated tobramycin. The strains used were the tobramycin susceptible PA056SJ and the tobramycin resistant PA086SJD. SLN nanoparticles presented lower antimicrobial activity than NLC nanoparticles, w/o/w nanoparticles had lower antimicrobial activity than the rest of formulations. For tobramycin-susceptible isolate was observed that both MICS and MBEC were slightly lower (1 or 2 logs) for nanoencapsulated tobramycin than for free drug. For the tobramycin-resistant isolate no differences in MIC and MBEC were observed among nanoparticles and free tobramycin. Time-kill experiments showed that NLC-tobramycin is more active than free and SLN-tobramycin against the susceptible strain. On the other hand, SLN-tobramycin has a slightly better activity than the NLC-tobramycin against the resistant strain, but free tobramycin activity is worse than both.

[1]Tarquinio K. Activity of tobramycin and polymixin-E against *P.aeruginosa* biofilm coated medical grade endotracheal tubes. *Antimicrob. Agents Chemother*. 10.1128/AAC.01178-13. 2014, **58**(3):1723.

[2]Luo Y, Hossain M, Wang C, Qiao Y, An J, Ma L, Su M. Targeted nanoparticles for enhanced X-ray radiation killing of multidrug-resistant bacteria. *Nanoscale.* 2013 Jan 21;**5**(2):687-94.