EDTA and Taurolidine affect *Pseudomonas aeruginosa* virulence *in vitro*: impairment of secretory profile and biofilm production onto peritoneal dialysis catheters

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Introduction: peritoneal catheter-associated biofilm infection is reported to be the main cause of refractory peritonitis in peritoneal dialysis patients. The application of antimicrobial lock therapy, based on results on central venous catheters, may be a promising option also for treatment of biofilm-harboring peritoneal catheters. In this study, we investigated the effects of two lock solutions, EDTA and Taurolidine, on an "*in-vitro*" model of *Pseudomonas aeruginosa* biofilm-related peritoneal catheter infection.

Materials and Methods: silicon peritoneal catheters were incubated for 24 h with a bioluminescent strain of *P. aeruginosa*. After washing, serial concentrations of Taurolidine (0.5, 0.25 and 0.125 %) and EDTA (2.5, 0.75 and 0.25 %), either alone or in combination, were applied for 24 h, once or twice, onto the contaminated catheters and then *P. aeruginosa* viability/persistence was evaluated in real time up to 120 h, by a Fluoroskan reader. Moreover, on selected supernatants from biofilm treated or not with EDTA and/or Taurolidine, High-Performance Liquid Chromatography-Mass (HPLC) analysis was performed to measure phenazine and pyocianine production.

Results: Taurolidine alone or in combination with EDTA caused a significant decrease of bacterial load and biofilm persistence onto the contaminated catheters. The lock solution treatment did not lead to the sterilization of the devices; yet, it resulted in a substantial destructuration of the peritoneal catheter-associated *P. aeruginosa* biofilm. Moreover, HPLC analysis showed that the treatment of biofilm-harboring catheters with EDTA and Taurolidine deeply affected the secretion of some key virulence-related molecules by *P. aeruginosa*, such as phenazines and pyocianines.

Discussion and conclusions: EDTA and Taurolidine affect the formation and persistence of *P. aeruginosa* biofilm onto peritoneal catheters; moreover, also the secretion of *P. aeruginosa* virulence factors is profoundly compromised. Future studies are needed to establish whether such

lock solutions can be used to render peritoneal catheter-related infections more susceptible to antibiotic treatment, thus avoiding/reducing the onset of the antibiotic resistance phenomena.