

Session: OS097 Biofilms: novel methods in treatment & prevention

Category: 9c. Preclinical biofilm studies

23 April 2017, 17:12 - 17:22
OS0503

The optimal regimen of ethanol lock therapy to treat biofilm-associated catheter infections: results from an in-vitro study

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Background: Catheter-related bloodstream infections (C-RBSI) can be managed without catheter removal in some situations where the maintenance of the catheter is essential. For these situations, the combination of systemic antimicrobials with antimicrobial catheter lock therapy (LT) is recommended. Alternatively, non antibiotic, and particularly ethanol solutions, are being used. However, there is no clear consensus on their use, due to controversies regarding efficacy, dosage, use of concomitant anticoagulants, and adverse effects. Our objective was to test in and in vitro model different combinations of ET lock solutions and heparin to find the most suitable regimen of ethanol lock therapy (ELT) using the minimum concentration of the components enough to eradicate biofilms of different microorganisms.

Material/methods: Three different concentrations (25%, 40% and 70%) of ET with and without 60UI of heparin, and three different periods of LT (2h, 24h and 72h) were tested against 24-hour biofilms of *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Enterococcus faecalis*, *Escherichia coli* and *Candida albicans* formed in a static, 96-well microtiter plate model. Efficacy of the ELT was calculated as the reduction of metabolic activity using tetrazolium salt (XTT). We also tested the efficacy of ELT to inhibit the 24-h re-growth of bacterial and fungal cells within the biofilm in a single-dose and a 7-day LT. Heparin activity was measured by Anti-Xa assay.

Results: Overall, we collected 270 experiments which showed that the best ethanol concentration enough to reduce >90% the metabolic activity of bacterial and fungal biofilms was 40%. The best

regimen of exposition of biofilms was 24h, which required the addition of heparin 60UI (without it being inactivated). Best percentages of re-growth inhibition were detected in ELT single-dose regimen. Details of each experiment are showed in the figure.

Conclusions: According to our in vitro data, ethanol lock solutions should contain 40% of ethanol + heparin 60UI and be maintained for 24 hours in a single dose for the treatment of biofilm formed infections. Future studies are needed to demonstrate its efficacy to treat C-RBSI in a clinical setting.

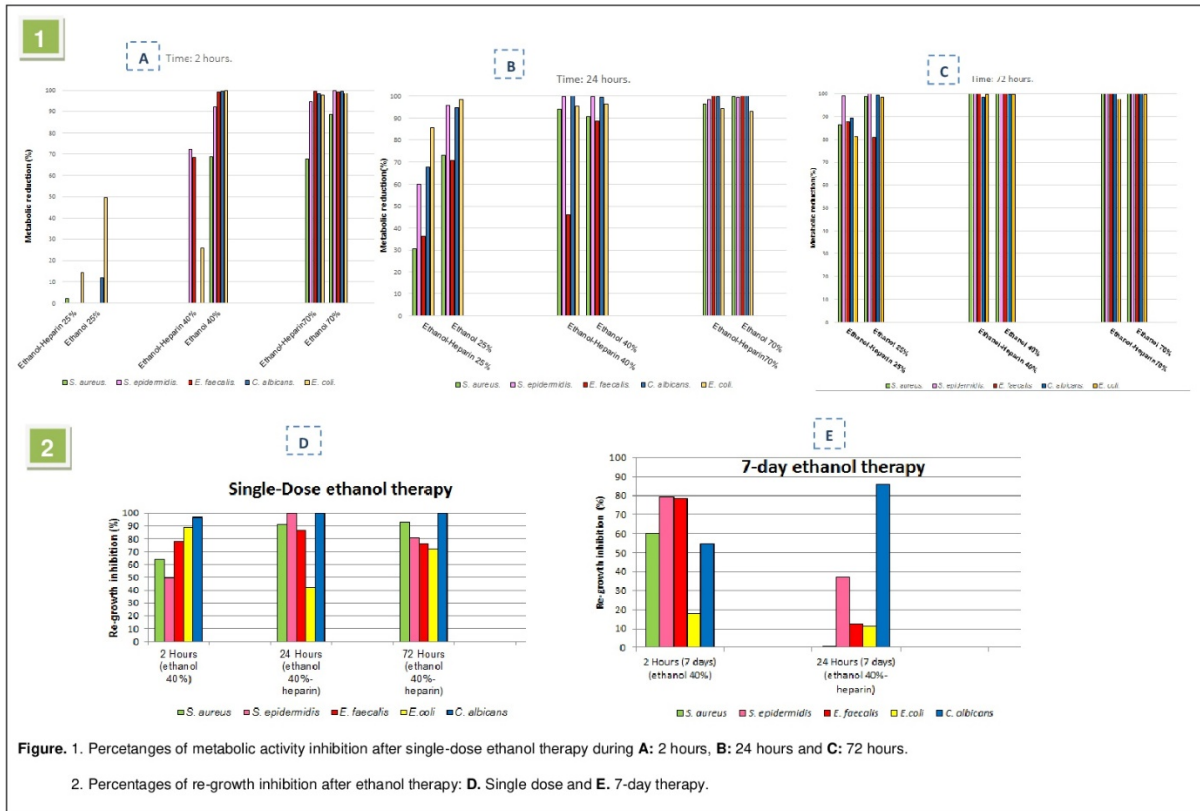


Figure 1. Percentages of metabolic activity inhibition after single-dose ethanol therapy during A: 2 hours, B: 24 hours and C: 72 hours.

2. Percentages of re-growth inhibition after ethanol therapy: D. Single dose and E. 7-day therapy.