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MEETING ABSTRACT

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Human bile reduces antimicrobial activity of selected antibiotics against *Escherichia coli* and *Enterococcus faecalis in vitro*

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Background: In antimicrobial drug development and clinical routine antibiotics are tested in standardised culture media. The impact of biological fluids like urine, cerebrospinal fluid or plasma, *i.e.* the site of bacterial infection, on antimicrobial activity was previously demonstrated. The present *in vitro* experiments investigated the effect of bile on bacterial killing of ciprofloxacin (CIP), meropenem (MEM), tigecycline (TGC) and linezolid (LZD) against *Escherichia coli* and *Enterococcus faecalis*.

Methods: Human bile was obtained from 11 patients who underwent cholecystectomy because of cholecystitis or cholecystolithiasis and sterilisation was achieved by gamma radiation. Time–kill curves of CIP, MEM and TGC against *E. coli* ATCC 25922, as well as LZD and TGC against *E. faecalis* ATCC 29212 were performed in pooled human bile and in Mueller-Hinton broth (MHB). For each compound and strain at least 4 concentrations were tested. Minimal Inhibitory concentrations (MICs) determined by broth microdilution method were conducted in MHB only.

Results: Human bile did not negatively affect bacterial growth over 24 hours. Bacterial counts (in CFU/ml after 24 hours) of bile growth controls were approximately equal to MHB growth controls for *E. coli* and 2.5-fold greater for *E. faecalis* indicating a promotion of bacterial growth for the latter strain. Bile reduced killing of CIP, MEM and TGC against *E. coli* and killing of LZD against *E. faecalis* considerably. This effect was strongest for TGC against *E. coli*.

Discussion: The present data indicate that bile inhibits antimicrobial activity of CIP, MEM, TGC and LZD against *E. coli* and *E. faecalis*, respectively. These findings may have important implications for the treatment of bacterial infections of the gallbladder and biliary tract, and should be explored in more detail.

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