Vancomycin has comparable efficacy in eliminating *Cutibacterium acnes* biofilm as doxycycline and penicillin in an in vitro model

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Background

- *Cutibacterium acnes* is a significant pathogen in periprosthetic joint infections (PJI) in Total Shoulder Arthroplasty (TSA). TSA infection rate ranges from 0.7-4%, up to 15% for revision arthroplasty.

- Poor outcomes seen in PJI are due to presence of established *C. acnes* bacterial biofilms. Extensive extracellular matrix structure and increased prevalence of metabolically inert "persister" cells results in chronic infections that are highly resistant to traditional antibiotics.

- Due to the prolonged nature of *C. acnes* infections, they are difficult to treat with antibiotics. *C. acnes* remains difficult to isolate due to long incubation period in culture. Biofilms are more difficult to isolate via synovial sampling methods.

Objective

- Determine the relative efficacy of vancomycin compared to penicillin and doxycycline against planktonic and mature biofilm cultures.

Hypothesis

- There will be a significant difference between the planktonic and biofilm inhibitory and bactericidal concentrations for vancomycin, doxycycline, and penicillin.

Methods

- Clinical registry *C. acnes* isolates from periprosthetic joint infection patients as well as a laboratory strain were tested against clinically administered antibiotics at varied logarithmic doses.

- Planktonic MIC and MBC were performed using modified CLSI assays. Cultured anaerobically for 3 days.

- Biofilms were grown for 7 days and minimum biofilm inhibitory concentration (MBIC) and minimum biofilm bactericidal concentration (MBBC) was performed.

- PrestoBlue viability stain was used to determine MIC and MBIC.

- CFU analysis using DRCM plates was used to find MBC and MBBC.

Variability in *C. acnes* sensitivity

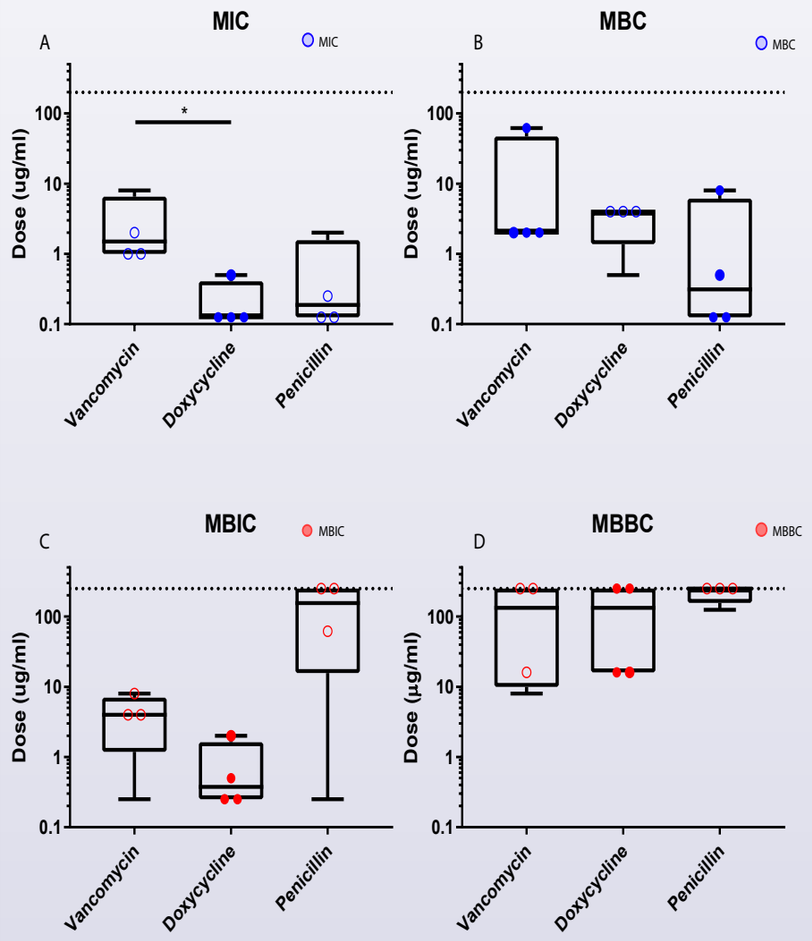

Figure 1. Across sampled isolates, *C. acnes* demonstrated a varying resistances in both planktonic (blue) and an increased resistance to biofilm (red) cultures. Minimum inhibtory concentrations were determined using a PrestoBlue fluorescence assay. When the MIC was collected, there was a statistically significant difference between the doses of vancomycin and doxycycline (A). To determine the minimum bactericidal concentration, a CFU analysis was performed using DRCM plates. The dashed line represents the maximum tested dose (250 ug/ml).

C. acnes biofilm shows increased tolerance

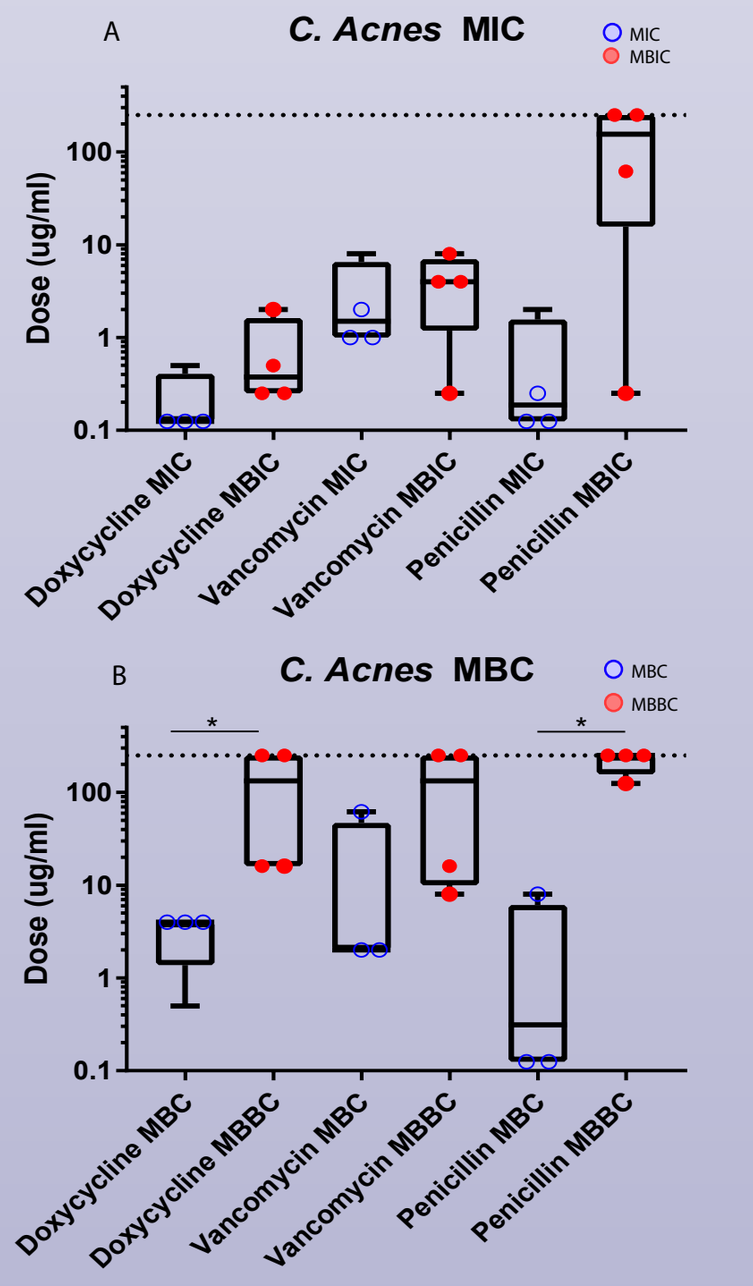

Figure 2. Sensitivity to antibiotics were compared between *C. acnes* strains grown planktonically compared to grown as mature biofilms. Doxycycline, vancomycin, and penicillin had similar inhibitory concentrations for both planktonic (MIC) and biofilm cultures (MBIC) (A). However, doxycycline and penicillin performed significantly worse at eradicating established biofilms (MBBC) than planktonic cultures (MBC) as denoted with the asterisks above (B). Vancomycin MBBC was higher than MBC, but did not reach statistical significance.

Results

- CLSI protocol and a mature biofilm in vitro model was used to quantify variation in planktonic MIC, planktonic MBC, biofilm MIC, and biofilm MBC across several *C. acnes* isolates.

- In the planktonic MIC group, vancomycin displayed significantly higher MIC than doxycycline (Fig 1A).

- All three antibiotics tested showed similar efficacy in planktonic cultures, with inhibitory and bactericidal concentrations within clinical dosing range (Fig 1A-B).

- Sensitivity to antibiotics were combared between *C. acnes* strains grown planktonically compared to grown as mature biofilms.

- There was no statistical significance between MIC and MBIC of doxycycline, vancomycin, and penicillin in the *C. acnes* strains tested (Fig 2A).

- Doxycycline and Penicillin demonstrated biofilm MBC values significantly higher than planktonic MBC values (Fig 2B).

Discussion

- Penicillin, doxycycline, and vancomycin demonstrated a similar ability to inhibit *C. acnes* bacterial growth in the planktonic state based on relative comparison of MIC and MBC.

- The MBIC for doxycycline and vancomycin was within clinical dosing ranges in all strains indicating minimal tolerance of *C. acnes* biofilm to these antibiotics and likely clinical efficacy with routine dosing.

- The MBIC for penicillin was within clinical dosing range in 25% of strains indicating relative tolerance of *C. acnes* to penicillin and possible clinical failure.

- Biofilm MBC for doxycycline and vancomycin showed efficacy at treament doses in 50% of tested samples, while penicillin showed efficacy at treatment doses in 0% of samples.

References