Minocycline activity against *Acinetobacter baumannii-calcoaceticus* species complex, *Burkholderia cepacia* complex, and *Stenotrophomonas maltophilia* from US hospitals

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Introduction

- *Acinetobacter baumannii-calcoaceticus* species complex (ACB), *Burkholderia cepacia* complex (BCC), and *Stenotrophomonas maltophilia* (SM) are opportunistic non-fermentative organisms that can cause serious hospital-acquired infections in immunocompromised patients.
- These pathogens are inherently resistant to several common drug classes and often acquire other resistance mechanisms, making them difficult to treat.
  - Options are particularly limited for BCC and SM, which have only 7 drugs with CLSI breakpoints.
- In this study, we analyzed the susceptibility of contemporary ACB, BCC, and SM isolates to minocycline, ceftazidime, levofloxacin, and trimethoprim-sulfamethoxazole.
  - Minocycline, levofloxacin, and trimethoprim-sulfamethoxazole are in CLSI M100 Table 1A (test and report) while ceftazidime is in Table 1B (test and report selectively) for SM.
- Isolates were collected as part of the SENTRY Antimicrobial Surveillance Program from 2017–2020.

Materials and Methods

- Isolates were collected from hospitalized patients in 33 US medical centers.
  - Hospitals submitted 1 isolate per patient per infection episode that met local criteria for being the likely causative pathogen.
  - All infection types were included in the analysis.
- Identification was performed by the submitting laboratory and confirmed by JMI Laboratories with matrix-assisted laser desorption ionization-time of flight mass spectrometry or other standard methods as required.
- Isolates were tested for susceptibility (S) to minocycline and comparators using the CLSI broth microdilution method.
  - CLSI (2021) breakpoints were applied.
- Multi-drug resistant (MDR) and extensively drug resistant (XDR) ACB isolates were also analyzed.
  - The MDR phenotype was defined as resistant to at least 1 agent in 3 or more drug classes (Magiorakos et al., 2012).
  - The XDR phenotype was defined as susceptible to agents in 2 or fewer drug classes.

Results

- The most common infection that ACB, BCC, and SM were isolated from was pneumonia in hospitalized patients (57.9%, 81.1%, and 73.9%, respectively), followed by skin and skin structure infections for ACB (21.5%) or bloodstream infections for BCC (13.5%) and SM (11.8%; Figure 1).
- The cumulative MIC distributions of minocycline for ACB, BCC, and SM are shown in Figure 2.
- The %S and $MIC_{50/90}$ values of the 4 drugs tested against the organisms in this study are shown in Table 1 for ACB and Table 2 for BCC and SM.
- Minocycline had the highest %S of tested antimicrobials for ACB (85.9%; Table 1).
- Minocycline was the most active agent tested against MDR (60.8%S) and XDR ACB (52.8%S).
  - MDR and XDR ACB were highly resistant to the other drugs tested.
- Minocycline was the most active antimicrobial against SM (99.3%S; Table 2).
  - SM susceptibility to trimethoprim-sulfamethoxazole was 95.8%.
  - 87.1% (27/31) of trimethoprim-sulfamethoxazole resistant SM isolates were minocycline susceptible.
- Ceftazidime had the highest %S (87.8%S) against BCC, while minocycline and trimethoprim-sulfamethoxazole had similar %S at 82.4%S and 83.8%S, respectively.

Conclusions

- Minocycline was the most active agent tested against ACB, including MDR and XDR isolates.
- Minocycline was the most active antimicrobial tested against SM.
  - Of the 31 trimethoprim-sulfamethoxazole resistant isolates, 87% were susceptible to minocycline.
- BCC had similar susceptibilities to minocycline and trimethoprim-sulfamethoxazole.
- These *in vitro* data suggest that minocycline may be a useful treatment option for infections caused by ACB, BCC, or SM.

Acknowledgements

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Table 1. Activities of minocycline and comparators when tested against *Acinetobacter baumannii-calcoaceticus* complex isolates, including MDR and XDR isolates

Organism/antimicrobial agent	MIC_{50}	MIC_{90}	CLSI[a] %S	%I	%R
Acinetobacter baumannii-calcoacetius species complex (n=489)					
Minocycline	0.25	8	85.9	4.5	9.6
Ceftazidime	8	>32	64.2	7.8	28.0
Levofloxacin	0.25	>16	65.8	0.2	33.9
Trimethoprim-sulfamethoxazole	≤0.5	>4	68.4		31.6
MDR (n=176)					
Minocycline	2	16	60.8	12.5	26.7
Ceftazidime	>32	>32	17.0	11.9	71.0
Levofloxacin	16	>16	5.7	0.6	93.8
Trimethoprim-sulfamethoxazole	>4	>4	22.7		77.3
XDR (n=125)					
Minocycline	4	16	52.8	13.6	33.6
Ceftazidime	>32	>32	13.6	8.0	78.4
Levofloxacin	>16	>16	0.0	0.8	99.2
Trimethoprim-sulfamethoxazole	>4	>4	16.0		84.0

[a] CLSI M100 (2021).

Table 2. Activities of minocycline and comparators against *B. cepacia* and *S. maltophilia*

Organism/antimicrobial agent	MIC_{50}	MIC_{90}	CLSI[a] %S	%I	%R
Burkholderia cepacia species complex (n=74)					
Minocycline	2	16	82.4	6.8	10.8
Ceftazidime	4	16	87.8	6.8	5.4
Levofloxacin	2	16	63.5	14.9	21.6
Trimethoprim-sulfamethoxazole	≤0.5	4	83.8		16.2
Stenotrophomonas maltophilia (n=742)					
Minocycline	0.5	2	99.3	0.7	0.0
Ceftazidime	>32	>32	20.2	9.6	70.2
Levofloxacin	1	8	75.5	10.6	13.9
Trimethoprim-sulfamethoxazole	≤0.5	1	95.8		4.2

[a] CLSI M100 (2021).

Figure 1. Isolates in this study by infection type

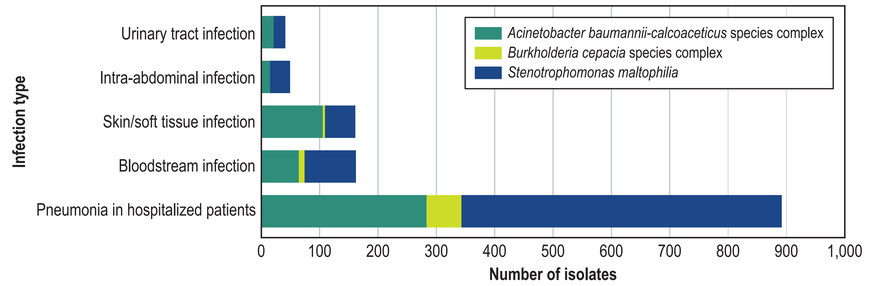

Figure 2. Cumulative percent MIC distributions of minocycline for the isolates in this study