High Dose Minocycline for the Treatment of *Acinetobacter* Infections

Shelbye R. Herbin, PharmD, BCPS; Amina Ammar, PharmD; Ryan Gumbleton, PharmD, BCCCP; Jing J. Zhao, PharmD; Shannon Olson, PharmD, BCIDP; Stephanie Smith, PharmD; Marco R. Scipione, PharmD, BCPS-AQ ID

Department of Pharmacy, Detroit Medical Center, Detroit, MI

Background

- Treatment options for *Acinetobacter* (ACB) include beta-lactams, fluroquinolones, aminoglycosides, polymyxins, or tetracyclines
  - Intrinsic and acquired resistance can make it difficult to treat and the CDC has classified Carbapenem-resistant ACB (CRAB) as an urgent threat
- Minocycline is a semi-synthetic derivative of tetracycline which has in-vitro activity against ACB including CRAB[1]
  - Minocycline has a favorable safety profile and is available both IV and PO
  - The optimal dose of minocycline for the treatment of ACB is unknown, however Monte Carlo simulations suggest that higher doses are required[2]
- Minocycline 200mg every 12 hours has been used at Detroit Medical Center (DMC) due to increased carbapenem resistance and toxicities associated with other therapies such as polymyxins

References:

1) Ritchie DJ and Garavaglia-Wilson A. A Review of Intravenous Minocycline for Treatment of Multidrug Resistant *Acinetobacter* Infections. *Clin Infect Dis* 2014; 59 (Suppl 6): S374-80.

2) Tsakris A, Koumaki V, Dokoumetzidis A. Minocycline susceptibility breakpoints for *Acinetobacter baumannii*: do we need to re-evaluate them? *J Antimicrob Chemother* 2019; 74 (2): 295-7.

Objective

- To compare treatment outcomes in patients with ACB infections who were given high-dose (HD) minocycline (MIN) 200mg every 12 hours or an alternative treatment option

Methods

- Patients admitted to DMC between January 1st 2019 and October 31st 2020
- **Inclusion criteria:** (1) ≥ 18 years old; (2) Positive culture for ACB
- **Exclusion criteria:** (1) ACB non-susceptible to MIN; (2) transferred to hospice w/in 72 hours of culture; (3) Positive ACB culture from urine only
- **Outcome Measures:**
  - Clinical success at the end of treatment (EOT)
    - Clinical success: complete resolution or improvement in signs and symptoms of infection
    - Clinical failure: lack of clinical improvement; or duration of treatment that exceeded 10 days for respiratory infections; or all-cause mortality
  - Microbiological success at EOT
    - Eradication of ACB from site of infection at EOT
  - Isolation of minocycline non-susceptible ACB w/in 30 days, adverse events associated with HD MIN

Results

Figure 1. Patient Screening

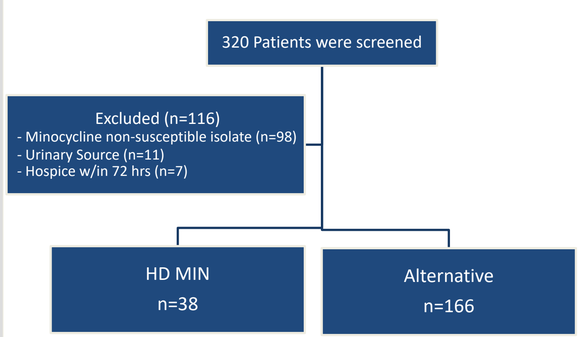

Table 1. Baseline Patient Characteristics

	HD MIN (n=38)	Alternative (n=166)	P-value
Gender, Male (%)	24 (63.2)	100 (60.2)	0.76
Age, Median (IQR)	41 (30.25-49.0)	40 (27.25-48.0)	0.50
Underlying Illness, n (%)			
Malignancy (Solid)	8 (21.2)	10 (6.02)	0.009
Peripheral Vascular Disease	2 (5.26)	13 (7.83)	0.84
Diabetes Mellitus	12 (31.6)	52 (31.3)	1.00
Chronic Kidney Disease	14 (36.8)	46 (27.7)	0.47
Congestive Heart Failure	10 (26.3)	18 (10.8)	0.03
Liver Disease	0 (0.00)	6 (3.61)	0.51
Malignancy (Hematologic)	0 (0.00)	6 (3.61)	0.51
Charlson Comorbidity Index, Median (IQR)	3 (1-4)	2 (1-4)	0.23
Indwelling Device, n (%)			
Urinary Catheter	23 (60.5)	99 (59.6)	1.00
Endotracheal Tube	6 (15.8)	33 (19.9)	0.73
Central Venous Catheter	5 (13.2)	19 (11.5)	0.99
Chest Tube	4 (10.5)	11 (6.6)	0.56

Table 2. Baseline Treatment Characteristics

	HD MIN (n=38)	Alternative (n=166)	P-value
Alternative treatment			
Cefepime	-	53 (32%)	
Meropenem	-	36 (22%)	
Ampicillin-sulbactam	-	24 (14%)	
Polymyxins	-	9 (5%	
Site of Infection			
Respiratory	23 (61%)	99 (60%)	1.00
Blood	6 (16%)	33 (20%)	0.73
Wound	5 (13%)	19 (12%)	0.99
Tissue	4 (11%)	11 (7%)	0.63
Fluid	0 (0%)	4 (2%)	0.75
Polymicrobial infection	28 (74%)	142 (86%)	0.13
Pseudomonas aeruginosa	9 (24%)	20 (12%)	0.11
Staphylococcus aureus	5 (13%)	29 (18%)	0.69
Candida spp.	5 (13%)	21 (13%)	1.00
Stenotrophomonas maltophilia	5 (13%)	11 (7%)	0.31
Proteus mirabilis	3 (8%)	16 (10%)	0.98
Length of stay, days, median (IQR)	16 (10.25-24.50)	14 (7-31)	0.99
Duration of therapy, days, median (IQR)	9 (6-11)	10 (2-18)	0.304
Time to appropriate therapy, hr, mean (SD)	70.2 (98.9)	28.2 (56.0)	0.02

Figure 2. Clinical Outcomes

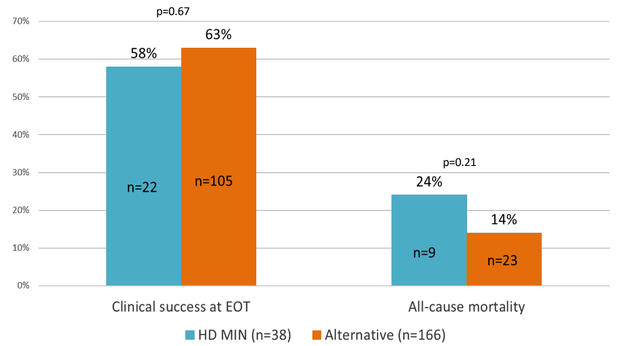

Figure 3. Microbiological Outcomes

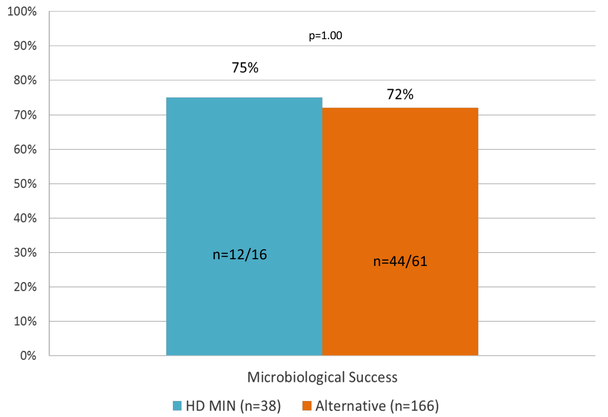

Table 3. Secondary Outcomes

	HD MIN	Alternative	P-value
DOT > 10 days for respiratory infection, n (%)	1/23 (4)	12/99 (12)	0.48
Minocycline Non-susceptible isolate w/in 30 days of EOT, n (%)	1/4 (25%)	3/17 (18%)	1.00
Readmission w/in 30 days, n (%)	7/38 (18%)	45/166 (27%)	0.37

Discussion

- Clinical and microbiological success were similar between patients who received HD MIN or alternative treatment
- All-cause mortality was numerically higher in those who received HD MIN
- There was a lower 30-day readmission rate in the HD MIN group
- Limitations: small sample size, and possibility ACB was a colonizer
- HD MIN may be an option for treatment of resistant ACB if other therapies are unavailable

Disclosure: Authors of this presentation have nothing to disclose concerning financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation.