Poster # 2415

Comparison of minocycline MIC's obtained by Etest to those obtained by broth microdilution in a bank of isolates of Acinetobacter baumannii collected in Southeastern Michigan

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Abstract

Background:
Minocycline is an important antibacterial for the management of Acinetobacter baumanii infections. Discordance in tigecycline susceptibilities between broth microdilution and Etest has been as high as 43% (a ≥ log 2 dilution higher MIC by ET). As many automated susceptibility panels do not include minocycline clinicians must rely on ET results. This analysis assesses the discordance between methodologies for minocycline and compares activity of minocycline and tigecycline against a clinical set of AB isolates from Southeast Michigan and Ohio.
Methods:
Testing using BMD and ET were done on 386 isolates of AB from 5 hospitals. Results were compared using FDA breakpoints with BMD considered the gold-standard. Correlations were defined as: (i) essential agreement (EA) if the ET MIC was identical to or 1 doubling dilution from the BMD MIC, (ii) categorical agreement (CA) if results via BMD and ET were the same susceptibility category, (iii) minor error if the isolate was intermediate by either test, but either susceptible or resistant by the other test, (iv) a major error if the isolate was false resistant by ET, and (v) a very major error if ET was false susceptible. Comparative BMD susceptibility between tigecycline and minocycline was also assessed.
Results:
Of the 386 isolates of AB, 87% were susceptible to minocycline by BMD and 77% by ET (9.6% difference, p <0.001). MIC comparisons are shown in Table 1. EA occurred in 82.9% of isolates and CA in 85%. Discordant results included 47 minor errors, 11 major errors, and 0 very major errors. 17% of isolates had >1 double dilution difference between the methodologies and 3.5% had > 2 double dilution differences. Susceptibility rates to tigecycline and minocycline were both 87% with no differences between susceptibility and nonsusceptibility.
Conclusion:
Minocycline provides excellent activity against AB. ET provides reliable susceptibility results in comparison to BMD.

Background

- Infections due to resistant Acinetobacter baumannii (AB) continue to rise.
- Antibiotics such as polymyxins and tigecycline retain activity, however are limited by toxicity, unachievable pharmacokinetics (pk) targets, heteroresistance, and challenges in susceptibility testing.
- Discordance in susceptibilities for tigecycline between broth microdilution (BMD) and Etest (ET) have been as high as 43% (a ≥ 2 $\log_{10}$ dilution higher MIC by ET).
- These limitations have led to a renewed interest in minoycline due to favorable pk, excellent invitro activity against AB; however it remains unclear if a similar testing discordance exists for minocycline.

Methods

- Testing using BMD and ET were done on 386 isolates of AB from 5 mid-west hospitals.
- Results were compared using FDA breakpoints with BMD considered the gold-standard.
- Correlations were defined as:
  - (i) Essential agreement if the ET MIC was identical to or 1 doubling dilution from the BMD MIC.
  - (ii) Categorical agreement (CA) if results via BMD and ET were the same susceptibility category.
  - (iii) Minor error if the isolate was intermediate by either test (MIC 8 mg/liter) but either susceptible (MIC ≤ 4 mg/liter) or resistant (MIC > 8 mg/liter) by the other.
  - (iv) A major error if the isolate was false resistant (non-susceptible) by ET (MIC > 8 mg/liter).
  - (v) A very major error if ET was false susceptible (MIC ≤ 4 mg/liter).
- Isolates that had more than one value on Etest that were not in the same range, were excluded.
- Etest results for minocycline were verified by two independent readers.
- Comparative BMD susceptibility between tigecycline and minocycline was assessed.
  - Tigecycline susceptible vs minocycline non-susceptible (MIC ≥ 8).
  - Minocycline susceptible vs tigecycline non-susceptible (MIC ≥ 4).

Results

Table1: Minocycline susceptibility comparing ET vs BMD

		Etest						
	MIC	≤0.25	0.5	1	2	4	8	>8
BMD n (%)	>8	0	0	0	0	0	0	18(4.7%)
	8	0	0	0	0	2(0.5%)	13(3.4%)	17 (4.4%)
	4	2 (0.5%)	0	1(0.25%)	3 (0.8%)	5(1.3%)	10(2.6%)	7(1.8%)
	2	0	1(0.25%)	2 (0.5%)	33 (8.5%)	15(1.3%)	11(2.8%)	2(0.5%)
	1	0	2 (0.5%)	14(3.6%)	78(20.2%)	20(5.2%)	7 (1.8%)	2 (0.5%)
	0.5	1(0.25%)	6 (1.6%)	14(3.6%)	6(1.6%)	0	0	0
	≤0.25	78(20.2%)	9 (2.3%)	5 (1.3%)	2(0.5%)	0	0	0

Table 2: Minocycline BMD vs Etest

BMD	S (</=4)	I (8)	R (>8)	Errors
	336/386	32/386	18/386	Minor 47/386 (12.2%)
	87%	8.3%	4.7%	Major 11/386 (2.8%)
Etest	S (</=4)	I (8)	R (>8)	Very Major 0/386 (0%)
	299/386	41/386	46/386	
	77.4%	10.6%	12%	

Results (Cont.)

Table 3: Tigecycline vs Minocycline BMD

		Minocycline BMD		
		S (</=4)	I (8)	R (>8)
Tigecycline BMD	S (</=2)	295/387 (76.2%)	27/387 (7.0%)	15/387 (3.9%)
	I (4)	28/387 (7.2%)	3/387 (0.8%)	0/387 (0%)
	R (>/=8)	15/387 (3.9%)	1/387 (0.3%)	3/387 (0.8%)

- 87% of Isolates (337/386 and 338/387) were susceptible to Tigecycline and Minocycline respectively.
- 11% of isolates (42/387) were susceptible to Tigecycline and non-susceptible to Minocycline.
- 11% of isolates (43/387) were susceptible to Minocycline and non-susceptible to Tigecycline.

Conclusions

- Minocycline provides excellent activity against AB.
- ET susceptibility provides reliable results in comparison to BMD (82.9% essential agreement and 85% categorical agreement).
- Additional BMD testing should be considered when ET results show minocycline resistance.
- Minocycline has equal activity to tigecycline for AB, with some minocycline susceptible isolates being resistant to tigecycline, as well as some minocycline resistant isolates being tigecycline susceptible.
- Additional studies evaluating the outcomes of minocycline in the treatment of resistant Acinetobacter infections are needed.