Poster 50

Surveillance of Iclaprim Activity: In Vitro Susceptibility of Drug-Susceptible and -Resistant Beta-hemolytic Streptococci Collected During 2012-2016 from Skin and Skin Structure Infections

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ABSTRACT

Background: Iclaprim is a diaminopyrimidine inhibitor of bacterial dihydrofolate reductase. Surveillance data collected prior to 2006 demonstrated that iclaprim was active against beta-hemolytic pathogens including emerging drug-resistant pathogens. In an era of increasing antimicrobial resistance, new agents that address bacterial resistance are needed. In the present study, iclaprim and comparator antibiotics were tested against drug-susceptible and -resistant beta-hemolytic streptococci from skin and skin structure infections, collected worldwide during 2012-2016.

Methods: 458 non-duplicative, non-consecutive isolates of beta-hemolytic streptococci (*Streptococcus pyogenes* [n=257]) and *S. agalactiae* [n=201]) underwent antibacterial susceptibility testing. Susceptibility testing was performed by broth microdilution in accordance with the Clinical and Laboratory and Standards Institute (CLSI) guidelines (CLSI M7). Minimum inhibitory concentrations (MIC) were interpreted using CLSI breakpoints (CLSI M100).

Results: The activity of iclaprim against drug-susceptible and -resistant subpopulations of *S. pyogenes* and *S. agalactiae* are shown in Table 1. Iclaprim had consistent and potent activity against *S. pyogenes* and *S. agalactiae* with $MIC_{50/90}$ (µg/mL) values against drug-susceptible that were identical or within 2-fold of those observed against -resistant isolates (with the exception of tetracycline-resistant *S. pyogenes*, where $MIC_{50/90}$ values were slightly higher relative to tetracycline-susceptible isolates).

Conclusion: Iclaprim was active against a 2012 to 2016 worldwide collection of drug-susceptible and drug-resistant beta-hemolytic streptococci from patients with skin and skin structure infections. Continued surveillance is warranted to monitor the activity of iclaprim against beta-hemolytic streptococci, as well as to detect any potential emergence of resistance.

INTRODUCTION

- Iclaprim is a novel diaminopyrimidine antibiotic, which inhibits bacterial dihydrofolate reductase, a critical enzyme in the bacterial folate synthesis pathway.
- Iclaprim is active against MRSA resistant to vancomycin or nonsusceptible to linezolid or daptomycin [1].
- Surveillance data collected from 2004 to 2006 demonstrated that iclaprim was active against beta-hemolytic pathogens including emerging drug-resistant pathogens [2].
- In the present study, iclaprim and comparator antibiotics were tested against drug-susceptible and -resistant beta-hemolytic streptococci from skin and skin structure infections, collected worldwide during 2012-2016 [3].

METHODS

- 458 non-duplicative, non-consecutive isolates of beta-hemolytic streptococci underwent antibacterial susceptibility testing including:
  - *Streptococcus pyogenes* (n=257)
  - *Streptococcus agalactiae* (n=201)
- Isolates were collected from the following regions:
  - Europe (n=205)
  - North America (n=204)
  - Latin America (n=26)
  - Asia Pacific (n=23)
- Susceptibility testing was performed by broth microdilution in accordance with the Clinical and Laboratory and Standards Institute (CLSI) guidelines (CLSI M7) [4].
- Minimum inhibitory concentrations (MIC) were interpreted using CLSI breakpoints (CLSI M100) [5]
  - Erythromycin (S ≤0.25, R ≥1 µg/mL)
  - Azithromycin (S ≤0.5, R ≥2 µg/mL)
  - Tetracycline (S ≤2, R ≥8 µg/mL)

RESULTS

- The activity of iclaprim against drug-susceptible and -resistant subpopulations of *S. pyogenes* and *S. agalactiae* are shown in Table 1.
- Iclaprim had consistent and potent activity against *S. pyogenes* in isolates that were either susceptible or resistant to erythromycin and azithromycin.
  - Compared with tetracycline-susceptible isolates, MIC_{50} and MIC_{90} (µg/mL) values were higher for iclaprim in isolates that were tetracycline-resistant *S. pyogenes*
- Iclaprim also had consistent and potent activity against *S. agalactiae*.
  - MIC_{50} and MIC_{90} (µg/mL) values against drug-susceptible isolates were identical or within 2-fold of those observed against erythromycin, azithromycin and tetracycline-resistant isolates.

Table 1. Activity of iclaprim against drug-susceptible and -resistant subpopulations of *S. pyogenes* and *S. agalactiae*.

Organism	Drug	Iclaprim Activity					
		Drug-Susceptible			Drug-Resistant		
		N	MIC_{50}	MIC_{90}	N	MIC_{50}	MIC_{90}
S. pyogenes	Erythromycin	83	≤0.015	0.06	13	≤0.015	0.03
	Azithromycin	133	≤0.015	0.03	24	≤0.015	0.03
	Tetracycline	229	≤0.015	0.06	125	0.06	0.5
S. agalactiae	Erythromycin	62	0.12	0.25	38	0.12	0.25
	Azithromycin	59	0.12	0.5	41	0.12	0.5
	Tetracycline	40	0.25	0.5	160	0.12	0.5

Abbreviations: MIC, minimum inhibitory concentration

CONCLUSIONS

- In an era of increasing antimicrobial resistance, new agents that address bacterial resistance are needed.
- Iclaprim was active against a worldwide collection of drug-susceptible and drug-resistant beta-hemolytic streptococci from patients with skin and skin structure infections from 2012 to 2016.
- Continued surveillance is warranted to monitor the activity of iclaprim against beta-hemolytic streptococci, as well as to detect any potential emergence of resistance.

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