ABSTRACT

Background: CBSN has conducted cross-Canada S. pneumoniae surveillance since 1987. During the last 5 years we have witnessed not only an increase in the prevalence of MDR (resistance to more than 2 classes of antibiotics) S. pneumoniae, but also an increase in the degree of R to the β-lactam antibiotics, including penicillin (PEN), amoxicillin (AMOX) and ceftriaxone.

Methods: To evaluate the activity of new antibiotics including ceftaroline, ceftobiprole, and cethromycin against MDR S. pneumoniae, we selected a representative sample of 219 isolates from 2003 to 2007. Susceptibility testing by broth-microdilution and broth-dilution methods was performed according to 2008 CLSI guidelines using the minimum inhibitory concentration (MIC) breakpoints (S: ≤2 μg/ml, I: 4 μg/ml, R: ≥8 μg/ml).

Results: Of 219 selected isolates, 25.5% were from blood, 35.6% from sputum, 14.7% from ear and 24.2% from other sites. In vitro susceptibility testing demonstrated that ceftaroline and ceftobiprole were more potent than cethromycin against both PEN S and NS isolates. Ceftaroline was the most active against PEN NS with MIC50 values 8-fold lower than cethromycin and 4-fold lower than ceftobiprole. The MIC50 of cethromycin was similar to telithromycin (0.03 μg/ml) against ERY S isolates and more potent against ERY R isolates with a 4-fold lower MIC50.

For this study, we selected from our database a representative sample of pneumococci between 2003 and 2007. We selected isolates that were considered multi-drug resistant as defined by resistance to 2 or more classes of drugs. In vitro susceptibility testing was performed by broth microdilution according to CLSI guidelines.

INTRODUCTION

The most commonly recommended antimicrobial drugs for treatment of S. pneumoniae are β-lactam agents ceftobiprole and ceftaroline, have wide spectrum of activity against gram-positive and gram-negative organisms including MRSA, S. pneumoniae and Enterobacteriaceae. A newly developed ketolide, cethromycin, also exhibits potent activity against macrolide resistant gram-positive bacteria.

METHODS AND MATERIALS

CBSN is comprised of over 100 volunteer groups of private and hospital-affiliated laboratories from across Canada. Since 1987, laboratories submit S. pneumoniae isolates as a part of a nation-wide surveillance program. Susceptibilities to all isolates submitted to a central location are assessed according to CLSI. In addition, isolates are serotyped.

RESULTS

Table 1. Characteristics of S. pneumoniae isolates.

Serotypes N (%) Year of Isolation # of Isolates (% of total) TFA TBF

2003 35 (16.1) (80) 297 (71.4)
2004 43 (19.7) (24.8) 258 (58.1)
2005 54 (24.8) (9.1) 285 (51.6)
2006 47 (21.6) (24.8) 275 (57.4)
2007 39 (17.9) (15.8) 174 (38.0)
Total 219* 39 122

Type Site

Non Sterile 157 (71.7)
Sterile 61 (27.9)

Age (yrs)

<15 80 (36.5)
16-64 73 (33.3)
≥65 64 (29.2)

Geographic Area

Western Canada (Alb, BC, SK) 13
Mandota 12
Ontario 145
Quebec 15
Eastern Canada (NF, NS, PEI) 33

Conclusion: Ceftaroline, ceftobiprole, and cethromycin demonstrate potent in vitro activities against MDR S. pneumoniae isolates and suggest that these drugs could become important in treating infections due to emerging β-lactam R S. pneumoniae isolates.

OBJECTIVE

To determine in vitro activities of ceftaroline, ceftobiprole and cethromycin against MDR S. pneumoniae isolates in Canada.

SUMMARY AND CONCLUSION

• Overall, 96.3% of isolates were R to PEN, 63.9% to AMOX, 68.9% to ceftriaxone and clindamycin, 92.7% to erythromycin (ERY) and trimethoprim, and 72.6% to tetracycline.
• The prevalence of serotype 19A among MDR isolates increased from 0% in 2003 to 38.5% in 2007.
• Overall, MIC50 of ceftaroline was 8 fold lower, and MIC90 of ceftriaxone was 2 fold lower compared with the MIC50 of ceftriaxone (2 μg/ml) (Table 2).
• MIC50 of cethromycin was 4 fold lower than MIC50 of telithromycin (0.5 μg/ml) (Table 2).
• Among PEN NS isolates, MIC50 of ceftriaxone (0.25 μg/ml) was 4-fold lower than ceftriaxone (2 μg/ml) and 4-fold lower than ceftobiprole (1 μg/ml) (Table in abstract).
• Among AMOX R isolates, ceftaroline and ceftobiprole were more potent with MIC50 of 1 μg/ml and 4 fold lower than MIC50 of ceftriaxone (4 μg/ml) (Table in abstract).
• MIC50 of cethromycin was 4 fold lower than that of telithromycin among ERY R isolates (Table 2).

Table 2. In vitro activities of new antimicrobial agents against S. pneumoniae isolates.

Minimal inhibitory Concentration (μg/ml) N (% of isolates)

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</tr>
</tbody>
</table>

Note: Bold values represent MIC50.
Yellow shaded boxes correspond to intermediate MIC values according to CLSI.
§MIC interpretive standards have not been established by CLSI.

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