In vitro activity of ceftaroline, ceftobiprole and cethromycin against clinical isolates of Streptococcus pneumoniae collected from across Canada between 2003 and 2008

Samir N. Patel1,2, Dylan R. Pillai2,3, Sylvia Pong-Porter1, Allison McGeer1,2, Karen Green1 and Donald E. Low1–3 *

1Department of Microbiology, Mount Sinai Hospital, Toronto, Ontario M5G 1L5, Canada; 2Department of Laboratory Medicine and Pathobiology, University of Toronto, Toronto, Ontario M5G 1L5, Canada; 3Ontario Public Health Laboratories, Toronto, Ontario M9P 3T1, Canada

Keywords: β-lactams, ketolides, multidrug-resistant, community-acquired pneumonia

Sir,

Streptococcus pneumoniae is an important cause of both invasive and non-invasive infections in all age groups throughout the world. While the introduction of pneumococcal conjugate vaccine led to a decrease in invasive pneumococcal disease, multidrug-resistant (MDR) strains not belonging to serotypes included in the vaccine are now increasing and may result in treatment failures, as predicted by pharmacokinetic and pharmacodynamic parameters.1,2

Ceftobiprole and ceftaroline are newly developed parenteral cephalosporins that exhibit broad-spectrum activity against Gram-positive, Gram-negative and anaerobic organisms, including S. pneumoniae and methicillin-resistant Staphylococcus aureus.3,4 Cethromycin is a new ketolide antimicrobial agent with in vitro activity against penicillin- and macrolide-resistant Gram-positive organisms, possibly due to a higher affinity for the target site on the ribosomal unit.5 The purpose of this study was to evaluate in vitro activities of ceftaroline, ceftobiprole, cethromycin and several other antimicrobial agents against clinical isolates of MDR S. pneumoniae strains submitted to the Canadian Bacterial Surveillance Network (CBSN) as part of an ongoing nationwide surveillance programme.

We retrospectively selected 260 MDR isolates submitted to CBSN from 2003 to 2008. Isolates were defined as MDR if they were non-susceptible to amoxicillin and two other classes of drugs. In vitro susceptibility testing was performed by both microdilution and breakpoint interpretations were as per CLSI guidelines.6 Of 260 selected isolates, 193 (74.2%) isolates were recovered from non-sterile specimens (113 sputum, 16 bronchial wash, 24 eye, 36 ear and 4 others) and 66 (25.4%) isolates were from sterile specimens (59 blood, 1 CSF and 6 others). The origin of one isolate was not known. Eighty-nine isolates (34.2%) were recovered from paediatric patients (0–15 years old), 98 (37.7%) from adults between 16 and 64 years of age, and 71 (27.3%) from adults aged ≥65 years. Age information for two isolates was not known. Overall, 85% (221/260) were non-susceptible to penicillin (non-meningitis parenteral breakpoint, MIC ≥ 4 mg/L), 100% were non-susceptible to amoxicillin (non-meningitis breakpoint, MIC ≥ 4 mg/L) and 73.5% (191/260) were non-susceptible to ceftriaxone (non-meningitis breakpoint, MIC ≥ 2 mg/L). In addition, 72.3% were resistant to clindamycin, 94.6% to erythromycin, 95.8% to trimethoprim/sulfamethoxazole and 75.4% to tetracycline.

In this study, 90.4% (235/260) of isolates were serotype 19F (n = 145), 19A (n = 60) or 14 (n = 30). Of note, 90% (18 out of 20) of emergent MDR 19A isolates tested in this study belonged to ST320 (CC271), a single-locus variant of the Taiwan 19F-14 strain that spread globally in the 1990s.

As shown in Table 1, ceftaroline, ceftobiprole and cethromycin were highly active against all MDR pneumococcal isolates. Overall, the MIC90s of ceftaroline (0.25 mg/L) and ceftobiprole (1 mg/L) were 8- and 2-fold lower, respectively, than the MIC90 of ceftriaxone (2 mg/L). Similarly, MIC90s of ceftaroline and ceftobiprole were 32- and 8-fold lower, respectively, than the MIC90 of amoxicillin (8 mg/L). Cethromycin, a new ketolide, and 64 years of age, and 71 (27.3%) from adults aged ≥65 years. Age information for two isolates was not known. Overall, 85% (221/260) were non-susceptible to penicillin (non-meningitis parenteral breakpoint, MIC ≥ 4 mg/L), 100% were non-susceptible to amoxicillin (non-meningitis breakpoint, MIC ≥ 4 mg/L) and 73.5% (191/260) were non-susceptible to ceftriaxone (non-meningitis breakpoint, MIC ≥ 2 mg/L). In addition, 72.3% were resistant to clindamycin, 94.6% to erythromycin, 95.8% to trimethoprim/sulfamethoxazole and 75.4% to tetracycline.

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Table 1. In vitro activities of new drugs against MDR pneumococcal isolates

<table>
<thead>
<tr>
<th>Drugs</th>
<th>MIC90 (mg/L)</th>
<th>MIC90 (mg/L)</th>
<th>Range (mg/L)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>PEN MIC ≥ 4 mg/L</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ceftriaxone</td>
<td>2.0</td>
<td>2.0</td>
<td>0.25–8.0</td>
<td>221</td>
</tr>
<tr>
<td>cefotaxime</td>
<td>0.25</td>
<td>0.25</td>
<td>0.12–0.5</td>
<td>221</td>
</tr>
<tr>
<td>ceftobiprole</td>
<td>0.5</td>
<td>1.0</td>
<td>0.25–2.0</td>
<td>221</td>
</tr>
<tr>
<td>telithromycin</td>
<td>0.5</td>
<td>0.5</td>
<td>0.01–1.0</td>
<td>175</td>
</tr>
<tr>
<td>cethromycin</td>
<td>0.12</td>
<td>0.12</td>
<td>0.02–0.5</td>
<td>260</td>
</tr>
<tr>
<td>ERY MIC ≥ 0.5 mg/L</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ceftriaxone</td>
<td>2.0</td>
<td>2.0</td>
<td>0.25–8.0</td>
<td>246</td>
</tr>
<tr>
<td>ceftaxime</td>
<td>0.12</td>
<td>0.25</td>
<td>0.12–0.5</td>
<td>246</td>
</tr>
<tr>
<td>ceftobiprole</td>
<td>0.5</td>
<td>1.0</td>
<td>0.25–2.0</td>
<td>246</td>
</tr>
<tr>
<td>telithromycin</td>
<td>0.5</td>
<td>0.5</td>
<td>0.01–1.0</td>
<td>196</td>
</tr>
<tr>
<td>cethromycin</td>
<td>0.12</td>
<td>0.12</td>
<td>0.01–0.5</td>
<td>245</td>
</tr>
</tbody>
</table>

PEN, penicillin; ERY, erythromycin.
also demonstrated increased potency compared with telithromycin, as the MIC$_{90}$ of cethromycin was 0.12 mg/L (4-fold lower) compared with an MIC$_{90}$ of telithromycin of 0.5 mg/L (Table 1).

Among penicillin-non-susceptible (MIC $\geq 4$ mg/L) isolates, the MIC$_{90}$ of ceftaroline was 0.25 mg/L and the MIC$_{90}$ of cefotiboprole was 1.0 mg/L, whereas that of ceftriaxone was 2 mg/L (Table 1). Similarly, the MIC$_{90}$ of cethromycin was 0.12 mg/L, which was 4-fold lower than that of telithromycin. Among erythromycin-non-susceptible (MIC $\geq 0.5$ mg/L) isolates, the MIC$_{90}$ of cethromycin was 0.12 mg/L compared with an MIC$_{90}$ of telithromycin of 0.5 mg/L (Table 1). Similarly, the results showed that ceftaroline, cefotiboprole and cethromycin were more active against emerging MDR serotype 19A than currently available drugs.

In summary, among β-lactams tested, ceftaroline was the most potent against MDR S. pneumoniae isolates. Similarly, the ketolide cethromycin was more active than telithromycin.

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References


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Transmission of methicillin-resistant Staphylococcus aureus strains between humans and dogs: two case reports

Ulrike Nienhoff1, Kristina Kadlec2, Iris F. Chaberny3, Jutta Verspohl4, Gerald-F. Gerlach4, Stefan Schwarz2*, Daniela Simon1 and Ingo Nolte1

1Small Animal Clinic, University of Veterinary Medicine Hannover, Hannover, Germany; 2Institute of Farm Animal Genetics, Friedrich-Loeffler-Institute (FLI), Neustadt-Mariensee, Germany; 3Institute of Medical Microbiology and Hospital Epidemiology, Hannover Medical School, Hannover, Germany; 4Institute for Microbiology and Infectious Diseases, University of Veterinary Medicine Hannover, Hannover, Germany

Keywords: molecular typing, MRSA, antibiotic resistance, zoonosis, pet animals, antimicrobial resistance

Sir,

Pet animals have been shown to act as a reservoir of antimicrobial-resistant bacteria, and transmission of methicillin-resistant Staphylococcus aureus (MRSA) between humans and animals has been described. For MRSA strains with a low host specificity, transfer is likely to occur in both directions between the humans and pets living in the same household. Dogs and cats have previously been reported to carry MRSA strains related to those of humans. To assess the presence of MRSA isolates among dogs and cats admitted to the Small Animal Clinic of the University of Veterinary Medicine Hannover, Germany, a survey was conducted during September 2007 to January 2008. Swabs were taken from the nose and the pharyngeal region as well as from the perineum of dogs and cats before they entered the clinic. In addition, a brief questionnaire for background information on the sampled pet and the pet owner was completed on a voluntary basis. In total, 803 dogs and 117 cats were sampled, among which only 3 dogs tested positive for MRSA. The two cases for which sufficient background data have been made available are presented.

Case 1

In September 2008, a 6-month-old female cross-bred dog weighing 5 kg was admitted to the Small Animal Clinic of the University of Veterinary Medicine Hannover for deciduous teeth extraction. The dog’s treatment history included a urinary tract infection in July 2008, which was successfully treated ambulantly with amoxicillin. At the time of sampling the dog did not show signs of an infection. For our study, an MRSA was cultured from the combined sample of the nose/throat. To find out from where the dog might have acquired the MRSA, samples