

Activity of ceftobiprole against clinically relevant strains of penicillin non-susceptible *S. pneumoniae*

* & I. Burckhardt, *K. Sebastian, *S. Zimmermann

*Department for Infectious Diseases, Med. Microbiology and Hygiene, University of Heidelberg, Heidelberg, Germany

&corresponding author: irene.burckhardt@med.uni-heidelberg.de

Introduction and Purpose

Ceftobiprole is a new parenteral cephalosporin and was successfully used in the treatment of pneumonia. It exhibits activity against many gram-positive organisms including *Streptococcus pneumoniae*. Activity against penicillin resistant strains of *S. pneumoniae* has been reported. Ceftobiprole can bind to PBP2a, PBP2b and PBP2x. EUCAST breakpoints for *S. pneumoniae* were published in 2015 (S ≤ 0.5 mg/L, R > 0.5 mg/L). We wanted to examine the in-vitro activity of ceftobiprole against a collection of penicillin non-susceptible *S. pneumoniae* clinical isolates (MIC ≥ 0.12 mg/L), compare it to the MIC values of penicillin, amoxicillin and cefotaxime and investigate a possible effect of incubation atmosphere (5% CO₂) on MIC values.

Materials and Methods

From February 2009 until November 2013 all clinically relevant penicillin non-susceptible strains of *S. pneumoniae* (MIC ≥ 0.12 mg/L) were stored at -80°C for further investigations. These strains were thawed and tested for ceftobiprole susceptibility using E-Test (Biomérieux and Liofilchem, 0.002-32 mg/L). All strains were tested as follows: MH-F, Biomérieux, o/n 36°C, +/- 5% CO₂. ATCC 49619 was used as quality control.

- 21 different penicillin non-susceptible *S. pneumoniae* strains could be identified.
- MIC for penicillin ranged from 0.12-4 mg/L. 8 strains originated from patients <18, 13 from patients ≥18. 13 patients were male, 8 were female.
- 2/3 of the strains were isolated from blood culture.
- MIC for ceftobiprole ranged between 0.006 and 0.38 mg/L, no resistant isolate was detected.
- Incubation atmosphere did not obviously influence MIC values
- Growth of 3 strains was dependent on the presence of 5% CO₂
- MIC values of penicillin correlated with MIC values of ceftobiprole.

material	No
blood	14
aspirate	1
eye	2
nose (CF)	3
tracheal secretion	1
Total	21

Table 1: Material distribution

Penicillin MIC	No
0.12	3
0.25	6
0.5	3
1	3
2	3
4	3
Total	21

Table 2: Penicillin MIC distribution

Results

Age (y)	No
<18	8
2	2
4	1
6	1
9	1
10	2
≥18	13
20	1
46	2
64	1
65	1
66	1
69	2
70	1
74	3
75	1

Table 3: Age distribution

Sex	No
Male	13
Female	8
Total	21

Table 4: Gender

Strain No	Penicillin MIC	Amoxicillin MIC	Cefotaxime MIC	Ceftobiprole MIC (CO ₂ , O ₂)	
Strain 1	0.12	0.06	0.03	0.008	0.008
Strain 2	0.12	0.06	0.06	0.008	0.008
Strain 3	0.12	0.015	0.015	0.006	no growth
Strain 4	0.25	0.03	0.06	0.012	0.016
Strain 5	0.25	0.015	0.03	0.008	0.008
Strain 6	0.25	0.12	0.06	0.016	0.023
Strain 7	0.25	0.12	0.25	0.032	0.023
Strain 8	0.25	0.03	0.06	0.008	0.008
Strain 9	0.25	0.25	0.12	0.008	0.008
Strain 10	0.5	0.06	0.25	0.023	0.023
Strain 11	0.5	0.25	0.5	0.125	no growth
Strain 12	0.5	0.25	0.5	0.19	no growth
Strain 13	1	0.12	0.06	0.32	0.32
Strain 14	1	0.12	0.12	0.064	0.032
Strain 15	1	1	1	0.125	0.094
Strain 16	2	1	1	0.125	0.125
Strain 17	2	1	0.5	0.125	0.125
Strain 18	2	2	1	0.38	0.19
Strain 19	4	4	2	0.25	0.25
Strain 20	4	8	1	0.38	0.38
Strain 21	4	4	2	0.38	0.38

Table 5: MIC distribution for penicillin, amoxicillin, cefotaxime and ceftobiprole

Conclusions

1. Penicillin non-susceptibility in *S. pneumoniae* is a rare event in Germany.
2. In all cases examined ceftobiprole would still be a treatment option since no resistant isolate could be identified.
3. The higher the MIC for penicillin, amoxicillin and cefotaxime the higher the MIC for ceftobiprole.