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Poster 1614

Dissociation of MIC distributions of amoxicillin and ceftaroline in a clinical collection of *S. pneumoniae* from respiratory tract infections

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Abstract (edited)

Background
Ceftaroline (CPT; active metabolite of the prodrug ceftaroline fosamil), is a recently approved broad spectrum cephalosporin with activity against *S. pneumoniae* including strains with resistance to other beta-lactams due to its affinity for PBP2x. Experience of CPT in Europe remains however limited. Our aim was to assess the susceptibility of *S. pneumoniae* obtained from patients with confirmed respiratory tract infection to CPT with special attention to strains with insusceptibility or resistance to AMX, using EUCAST interpretation criteria.

Methods
Isolates (n=155) were obtained from Belgium and Germany and included patients with community-acquired pneumonia and acute exacerbations of COPD. MICs were determined in cation-adjusted Mueller-Hinton broth supplemented with horse blood, using *S. pneumoniae* strain ATCC 49619 as quality control and with re-identification of each isolate by the optochin test.

Results
We present the cumulative MIC distributions of CPT and AMX in the collection analyzed. A clear dissociation was seen for isolates with an MIC > 0.0625 mg/L. For about 20 % of isolates, the MIC of AMX was higher than the S breakpoint of EUCAST (mostly driven by samples from patients with a history of COPD) whereas the MIC of CPT exceeded the EUCAST S breakpoint for only 2 % of the isolates.

Conclusions
In this collection of clinical isolates from patients with respiratory tract infections in two adjacent European countries, CPT shows a more favorable MIC profile than AMX when considering strains for which AMX shows elevated MICs.

References

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Acknowledgments

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Introduction and Aims

Ceftaroline is a newly developed cephalosporin with activity against S. *pneumoniae* isolates resistant (or non-susceptible) to penicillins, conventional cephalosporins and carbapenems thanks to its high affinity for PBP2x/2a/2b (1).

Ceftaroline has proven efficacious and safe in phase III trials dealing with community acquired pneumonia (CAP) (2), with "by-pathogen" microbiological response rates similar or better than those of ceftriaxone. Amoxicillin, however, is the commonly recommended antibiotic in Belgium and Germany for this type of infection. This leaves the clinician uncertain about the potential usefulness of ceftaroline in these local markets.

Repeating clinical trials of antibiotics for every antibiotic / market combination is financially very difficult and scientifically and ethically questionable. However, comparison of MIC distributions using appropriate breakpoints may provide evidence for suitability of an antibiotic in a given target market.

The present report aims at providing such evidence for ceftaroline *vs.* amoxicillin for *S. pneumoniae* infections in the Belgo-German environment.

Materials and Methods

Strains: two collections of isolates obtained between 2009 and 2012 from patients in Belgium and Germany with clinically confirmed diagnostic of community-acquired pneumonia and/or bacterial exacerbations of chronic bronchitis (n=155).

MIC determinations: cation-adjusted Mueller-Hinton broth supplemented with horse blood, with ATCC 49619 as quality control and with re-identification of each isolate by optochin test (3) and interpretative criteria of EUCAST (http://www.eucast.org).

Analysis: linear regressions (Prism [GraphPad software]) and quantile contour analysis (JMP [SAS]).

Results

Figure 1: cumulative MIC distributions

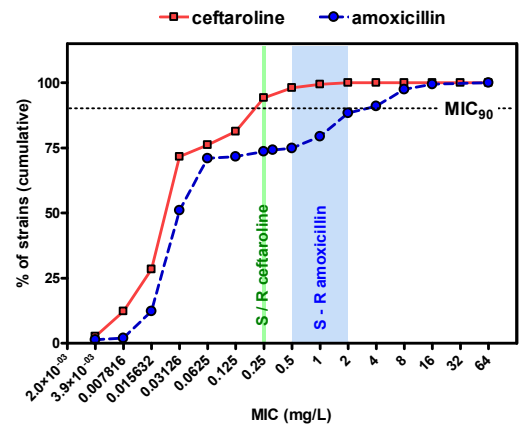
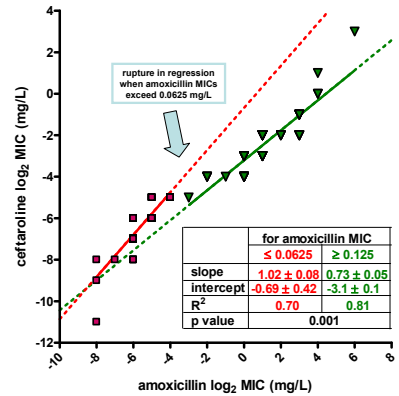
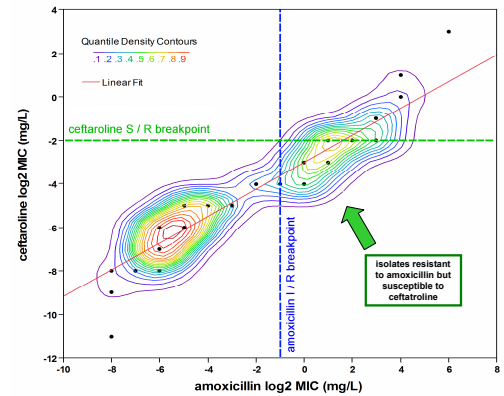


Figure 2: correlation analyses

A. Linear regressions
(one symbol may correspond to several isolates (1 to 23)



B. quantile density contour analysis
(colours indicate the proportion of strains)



Discussion

- In this collection including a sufficient proportion of isolates with reduced susceptibility to amoxicillin (EUCAST breakpoints), a clear advantage of ceftaroline can be demonstrated for these isolates.
- Breakpoints are set to allow categorizing organisms by a level of antimicrobial activity associated with high likelihood of therapeutic success or failure.
- Ceftaroline is, therefore, a useful addition to our current armamentarium (in approved indications) when and where amoxicllin susceptibility is decreased.
- Surveillance of ceftaroline susceptibility is warranted.

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