Epidemiological survey of antibiotic resistance in a Belgian collection of CAP isolates of *Streptococcus pneumoniae* (SP)

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Revised abstract

Objectives: Evaluate current resistance trends in SP (including efflux) towards the main classes of antibiotics used in the treatment of CAP.

Methods: Collection of SP (n=146) isolated from patients upon hospitalization for CAP in 4 Belgian hospitals over the last 2 years. MIC determined by microdilution in CAMH broth + 2.5% horse blood using reporter antibiotics (penicillin-G [PEN], erythromycin [ERY; clindamycin to detect efflux], and ciprofloxacin [CIP; ± reserpine]). Susceptibility assessed according to EUCAST and CLSI breakpoints.

Results:

AB	MIC_{50}	MIC_{90}	Range		EUCAST [a]		CLSI [b]	
			min	max	% I	% R	% I	% R
PEN	0.063	2	?0.016	4	na	6.2	6.2	0
ERY	0.25	>32	?0.06	>32	6.2	35.6	6.8	34.9
CIP	1	1.5	0.25	16	95.2	4.8		
CIP + res[c]	0.5	0.75	0.125	12	97.9	1.4		

[a] EUCAST bkpts : PEN (proposed) : S≤2, R>2 ; ERY (proposed) : S≤0.25, R>0.5 ; CLI (proposed) : S≤0.5, R>0.5 ; CIP (published) : S≤0.125, R>2.
[b] CLSI bkpts : PEN : S≤2, R≥8 ; ERY & CLI : S≤0.25, R≥1 ; CIP : no bkpt proposed.
[c] reserpine conc.: 10 mg/L

A significant proportion of isolates could be categorized as PEN-R using EUCAST bkpts but would appear PEN-I according to CLSI. More than 35 % of isolates were resistant to macrolides, among which 21 % [7.5 % of the total of isolates] were clindamycin-susceptible (denoting efflux). Almost all isolates were of intermediate susceptibility to ciprofloxacin, with most of them showing a decreased MIC (1-2 dil.) in the presence of reserpine (denoting efflux).

Conclusion: The data confirm the decreased susceptibility of SP to beta-lactams (including the occurrence of fully-resistant strains, stressing the importance of the choice of breakpoint value), as well as the high prevalence of methylation-related resistance to macrolides in the community. They also show a significant impact of efflux on macrolide susceptibility and suggest a high prevalence of efflux mechanism(s) towards ciprofloxacin.

Introduction

Respiratory tract infections represent the major reason for antibiotic prescription out of the hospital. It is therefore not surprizing that the incidence of *S. pneumoniae* isolates with reduced susceptibility to antibiotics is increasing worldwide (1). In this respect, resistance by active efflux of the drugs has been for long underestimated, but appears today as a frequent determinant in resistance to macrolides (2) or quinolones (3).

Streptococcus pneumoniae is the most frequent pathogen associated with respiratory tract infections, including in community-acquired pneumonia (CAP). This infection requires optimal antibiotic therapy especially in patients at risk.

Epidemiological surveys are therefore needed to determine the local prevalence of resistance and to propose on this basis appropriate guidelines for treatment.

Aims of the study

- To evaluate current resistance trends
  - in a collection of *S. pneumoniae* isolated from CAP patients hospitalized in 4 major hospitals from the Brussels area
  - towards three main antibiotic classes (β-lactams, macrolides, quinolones).
- To evaluate the prevalence of efflux for macrolides and fluoroquinolones

Methods

- **Bacteria:** 146 strains of *S. pneumoniae* have been isolated over the 2004-2007 period from patients admitted in 4 major hospitals from the Brussels area, with a diagnosis of CAP (confirmed by in- depth analysis of the dossier).

- **Susceptibility testing:**
  MICs were determined by the microdilution method following CLSI recommendations.
  One reporter antibiotic was selected in each class for its high susceptibility to resistance mechanisms (penicillin-G [PEN], erythromycin [ERY], and ciprofloxacin [CIP]).
  S. pneumoniae ATCC 49619 was used as quality control. Susceptibility was assessed according to EUCAST and CLSI breakpoints.
- **Resistance due to active efflux** was evidenced
  - for macrolides, by comparing the MICs of ERY and clindamycin [CLI], the later being not substrate for Mef macrolide transporters but being affected by ribosomal mutations to the same extent as macrolides (4).
  - for quinolones, by determining the effect of reserpine (10 mg/L; inhibitor of quinolone efflux pumps) on ciprofloxacin MIC (5).

Conclusion

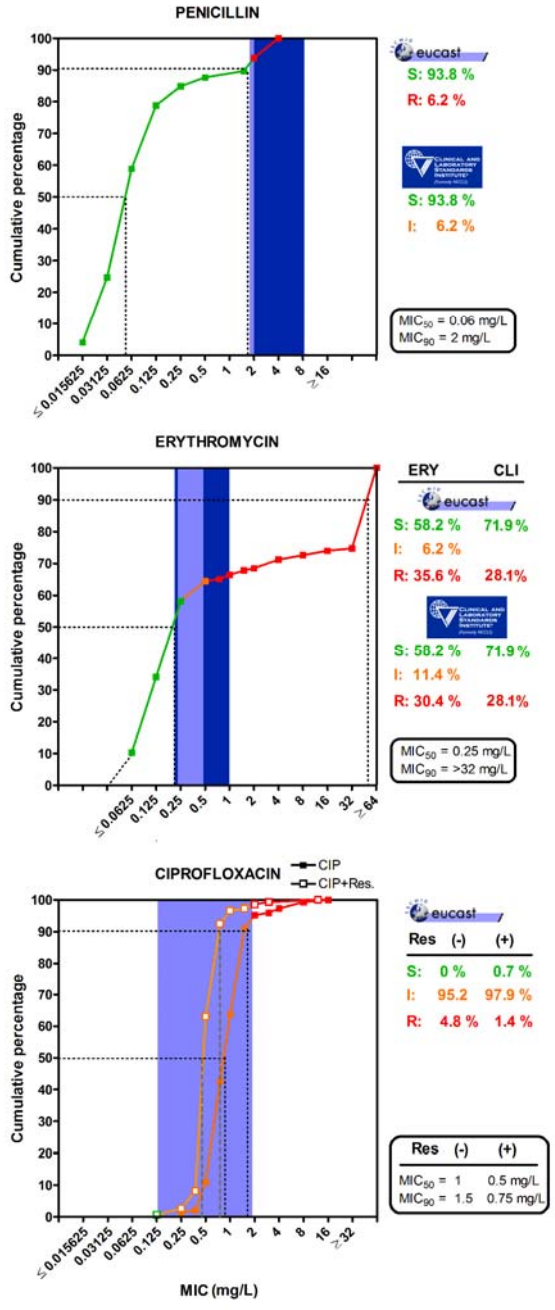
- **β-lactams:** the decreased susceptibility of *S. pneumoniae,* including the occurrence of fully-resistant strains (based on EUCAST breakpoints), was confirmed, stressing the importance of the choice of breakpoint values.
- **Macrolides:** a high prevalence of resistance was observed, which was due to ribosomal methylation in most of the cases. Efflux was not negligible, however, being responsible for loss of susceptibility in 1/5 of the resistant strains.
- **Quinolones:** ciprofloxacin was poorly active on the whole collection. Most of the strains were sensitive to reserpine, suggesting a high prevalence of efflux mechanism towards this class of antibiotics.

These data underline the risk of empirical treatment for CAP and plead for the importance of setting appropriate breakpoints based on PK/PD considerations for optimizing chances of therapeutic success.

This poster will be made available for download after the meeting at : http://www.facm.ucl.ac.be/posters.htm

Results

cumulative MIC distribution for 146 isolates of *S. pneumoniae* towards penicillin, erythromycin and ciprofloxacin.



Susceptibility (**EUCAST**): S: susceptible (green), I: intermediate (orange), R: resistant (red). AB alone (closed), + reserpine 10mg/L (open). Range tested delimited by symbols ≤ and ≥.
EUCAST breakpoints (zone for intermediate strains in light blue) : PEN (proposed) : S≤2, R>2 ; ERY (proposed) : S≤0.25, R>0.5 ; CLI (proposed) : S≤0.5, R>0.5 ; CIP (published) : S≤0.125, R>2.
CLSI breakpoints (zone for intermediate strains in dark blue): PEN : S≤2, R≥8 ; ERY & CLI : S≤0.25, R≥1 ; CIP : none proposed.

References

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