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Comparative in vitro activity of temocillin, meropenem, ceftazidime and piperacillin/tazobactam against panel strains and clinical isolates of *Burkholderia cepacia complex* from 9 different genomovars.

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ABSTRACT

Purpose. *B. cepacia* infection in cystic fibrosis (CF) patient is associated with increased morbidity and mortality. Temocillin (TMO), a semisynthetic 6-α-methoxy β-lactam, has already been successfully used in pilot studies for the treatment of pulmonary infections in CF patients infected with *B. cepacia*. We determined the susceptibility of well characterized panel strains and clinical isolates of *B. cepacia complex* to TMO in comparison with 3 other β-lactams used in CF patients : meropenem (MER), ceftazidime (CTZ), and piperacillin/tazobactam (PTZ).

Methods. The MICs were measured by microdilution in Mueller-Hinton broth using the CLSI method. *Pseudomonas aeruginosa* ATCC 27853 and *Escherichia coli* ATCC 25922 were included as control strains. CLSI breakpoints for Enterobacteriaceae were used for MER , CTZ, and PTZ and that of Fuchs *et al.* (1985 Eur J Clin Microbiol 4:30-33) for TMO.

Results. The table below shows the MIC50 and MIC90 obtained on 100 strains of *B. cepacia* from 9 genomovars of the complex (n= 30 and 35 for genomovars II and III, respectively, and 5 for genomovars I, and IV to IX).

β-lactam	MIC50 µg/ml	MIC90 µg/ml	Breakpoint µg/ml	% susceptibility %
TMO	8	32	16	81
MER	4	16	4	66
CTZ	4	> 128	8	70
PTZ	16	> 128	16	51

The susceptibility pattern was similar among the different genomovars. Interestingly, 7 strains were susceptible only to TMO, while 6/35 *B. multivorans* and 7/30 *B. cenocepacia* were resistant to all the antimicrobials tested,

Conclusion. TMO was active against more strains than any of the 3 other comparators. Combined with the results of the clinical pilot studies, our data suggest a potential therapeutic use for TMO in CF patients infected with *B. cepacia* complex strains.

METHODS

MICs were mesured by broth microdilution using the CLSI method. *Pseudomonas aeruginosa* ATCC 27853 and *Escherichia coli* ATCC 25922 were included as control strains. All control values were within recommendations. CLSI breakpoints for Enterobacteriaceae were used for MER, CTZ and PTZ, and the value proposed by Fuchs *et al.* for TMO (je donnerais les valeurs !!!)

INTRODUCTION and OBJECTIVE

CF is caused by mutations in a gene encoding a protein named CFTR which functions as a chloride channel in epithelial membranes [Collins, 1992]. The most dramatic changes are observed in CF airways causing chronic pulmonary infections with surprisingly few bacterial pathogens : *Pseudomonas aeruginosa* (most common isolate), *Staphylococcus aureus*, *Stenotrophomonas maltophilia* and *Burkholderia cepacia* [CFF Annual Report, 2002].

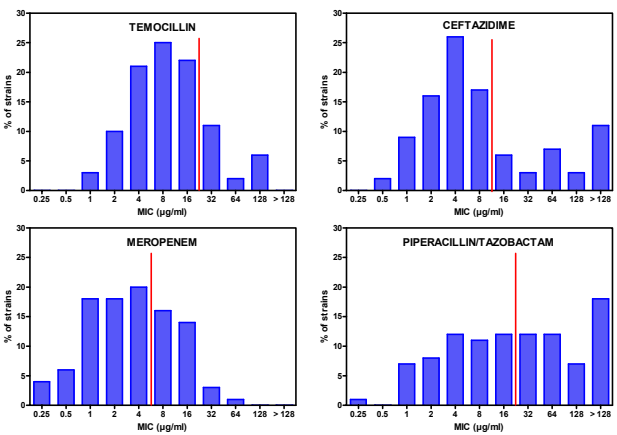
The *B. cepacia complex* (*Bcc*) represents at least 9 distinct bacterial species or "genomovars". *Bcc* are found in soil and on plants. The identification of unique *Bcc* strains CF sputum isolates implies acquisition from unknown reservoirs. The global prevalence rate among CF patients is around 3% (with up to 8% in adults) (Saiman and Siegel, 2003). Infections with *Bcc* are regarded as crucial for CF patients because in about one third of patients it causes a rapid decline of lung function, with as consequence, a dramatic reduction of life expectancy (up to 50%) (Corey and Farewell, 1996).

Although temocillin has already been used in a pilot clinical studies (Taylor *et al.*, 1992) with success for the treatment of *Bcc* infections in CF patients, only a few *in vitro* susceptibility data are available.

Our aim was, therefore, to determine the MICs of antibiotic used in CF patients (meropenem [MER], ceftazidime [CTZ], and piperacillin/tazobactam [PTZ]) in comparison with that of temocillin (TMO) towards a well characterized panel of laboratory strains and clinical isolates of *B. cepacia complex*.

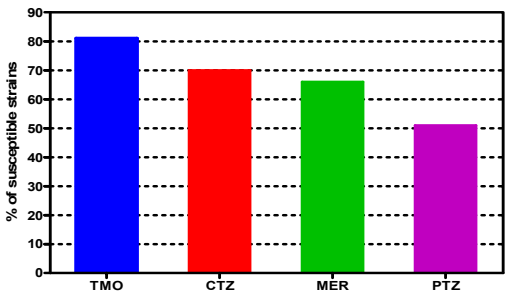
RESULTS

Figure 1 shows the MIC distributions of TMO, CTZ, MER, and PTZ against all 100 strains of *B. cepacia complex*.
The red line correspond to the CLSI breakpoint for CTZ, MER, and PTZ and that of Fuchs *et al.* for TMO



- No major differences were observed among the different genomovars
- No significant differences between the susceptibility patterns of panel strains and clinical isolates were observed

Figure 2 shows the global susceptibility of all strains to the 4 different β-lactams investigated



Some strains were extremely resistant while 7 strains were susceptible only to temocillin. Table 1 describes these particular strains

strains	nbr of strains	Genomovars
resistant to all antibiotics	**13**	**II (6) and III (7)**
susceptible only to TMO	**7**	**I (1), III (5), and VI (1)**
CTZ	**3**	**II**
MER	**1**	**V**
PTZ	**1**	**II**

CONCLUSIONS

- **TMO active against more *B. cepacia complex* strains compared to other clinically used β-lactams.**
- **These results, combined with those of pilot clinical studies, suggest a potential advantage of TMO in *B. cepacia* infected CF patients**

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