Temocillin : an alternative to carbapenem for multi-drug resistant *Enterobacteriaceae* ?

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Background

Treatment options for Multi-Drug Resistant (MDR) Gram Negative bacteria are scarce. In this context, temocillin, a 6-α-methoxy derivative of ticarcillin, represents an interesting option. Indeed, temocillin is stable against hydrolysis by most β-lactamases, including ESBLs and AmpC type β-lactamases. The aim of our study was to test the susceptibility of Enterobacteriaceae strains isolated in the University Hospital of Angers to temocillin, in order to evaluate the interest of this antibiotic as an alternative to carbapenems.

Material/Methods

- Susceptibility to temocillin was determined using the VITEK® 2 N-254 AST Card (bioMérieux), available in some European countries, but not in France
- 117 Enterobacteriaceae strains, isolated between March 2015 and September 2016, were studied retrospectively
- Susceptibility results were interpreted according to French recommendations (CASFM) (breakpoints : susceptible MIC ≤ 8mg/L, resistant MIC > 8 mg/L) Furthermore, infections associated with ESBL and derepressed AmpC isolates (29 cases) were reviewed for antibiotic therapy

Results

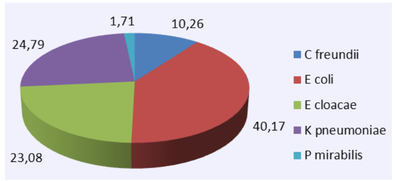

Figure 1 : Distribution of Enterobacteriaceae species included in this study (%)

- The 117 strains included *Escherichia coli* (40%), *Klebsiella pneumoniae* (25%), *Enterobacter cloacae* (23%), *Citrobacter freundii* (10%) and *Proteus mirabilis* (2%) (**Figure 1**)
- 34% of the strains were expressing ESBL (combined discs Neo-sensitabs® (ROSCO diagnostica)), 27% OXA-48 (Xpert® Carba-R (Cepheid)), 26% derepressed AmpC (AmpC confirm ID kit® (ROSCO diagnostica)), 9% were wild type isolates (WT), 3% were expressing penicillinases (AES system (bioMérieux)) and 1% KPC (Xpert® Carba-R) (**Figure 2**)

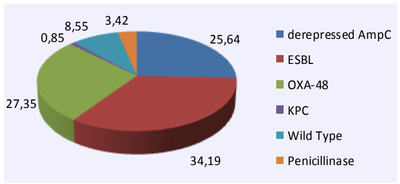

Figure 2 : Distribution of resistance mechanisms in Enterobacteriaceae (%)

- Temocillin demonstrated an excellent activity against WT isolates (100% susceptible)
- No efficacy was observed on carbapenemase-producing strains (MIC > 16 mg/L)
- 50% of Penicillinase-producing isolates were susceptible to temocillin (MIC ≤ 4 mg/L)

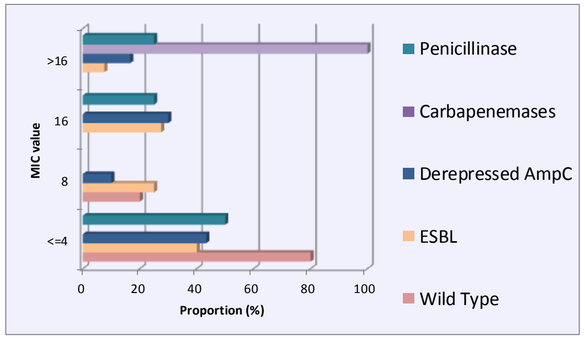

Figure 3 : Distribution of temocillin MICs according to the resistance mechanism

- Concerning ESBL positive isolates, 65% were susceptible to temocillin (40% with MIC ≤ 4 mg/L). Among them, all CTX-M producing isolates (6) were susceptible, with a MIC ≤ 4 mg/L
- Derepressed AmpC-producing isolates were for 53% susceptible to temocillin
- Within the 29 records of infections associated with ESBL or derepressed AmpC isolates, 24% were treated by carbapenems whereas they were susceptible to temocillin.

Conclusions

Temocillin is an antibiotic proposed as a therapeutic agent on MDR Enterobacteriaceae. The aim of this study was to test the susceptibility to this antibiotic on strains isolated in the University Hospital of Angers, in order to evaluate the impact as an alternative to carbapenems.

Here, 65% of ESBL-producing isolates and 53% of derepressed AmpC-producing isolates were susceptible to this antibiotic. 24% of infections associated with these bacteria could have been treated by temocillin instead of a carbapenem. This result assesses that temocillin is an alternative to carbapenems for some infections due to ESBL and derepressed AmpC producing Enterobacteriaceae.

However, the rates of susceptibility within these strains, and the lack of activity of this antibiotic against OXA-48 producing strains makes this molecule hardly usable in a probabilistic antibiotherapy, depending on the local resistance epidemiology.