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Temocillin : an alternative to carbapenems for multidrug-resistant Enterobacteriaceae ?

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Background: Treatment options for Multi-Drug Resistant (MDR) Gram Negative bacteria are scarce. Thus, temocillin represents an interesting option in this context. 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 carbapenem.

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, including *Escherichia coli* (40%), *Klebsiella pneumoniae* (25%), *Enterobacter cloacae* (23%), *Citrobacter freundii* (10%) and *Proteus mirabilis* (2%). Within these isolates, 34% were expressing ESBL (determined by combined discs Neo-sensitabs® (ROSCO diagnostica)), 27% OXA-48 carbapenemases (determined by Xpert® Carba-R (Cepheid)), 26% derepressed AmpC (determined by AmpC confirm ID kit® (ROSCO diagnostica)), 9% were wild type isolates (WT), 3% were expressing penicillinases (analysed by AES system (bioMérieux)) and 1% KPC (determined by Xpert® Carba-R (Cepheid)). Susceptibility results were interpreted according to the recommendations of the

French Society for Microbiology (CASFM). Furthermore, infections associated with ESBL and derepressed AmpC isolates selected for this study (29 cases) were reviewed for antibiotic therapy.

Results: Temocillin demonstrated an excellent activity against WT isolates (100% susceptible, and 80% with MIC ≤ 4 mg/L). No efficacy was observed on carbapenemases-producing strains (MIC > 16 mg/L). Penicillinase producing isolates were for a half susceptible to temocillin (MIC ≤ 4 mg/L). Within ESBL positive isolates, 65% were susceptible to temocillin (40% with MIC ≤ 4 mg/L). Among these ones, all CTX-M producing isolates (6) were susceptible to temocillin (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 and 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 carbapenem. 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 Enterobacteriaceae makes this one hardly usable in a probabilistic antibiotherapy, depending on the local resistance epidemiology.