Evaluation of doripenem in vitro activity in comparison with other carbapenems on carbapenem-resistant clinical isolates of Pseudomonas aeruginosa from a French multicenter study

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Background

P. aeruginosa remains a serious challenge in intensive care units. Carbapenem resistance is increasing. Doripenem, a more recent carbapenem active against P. aeruginosa has been recently withdrawn from the European market. The objective of this study was to assess the in vitro activity of doripenem in comparison to other carbapenems on clinical strains of carbapenem-resistant P. aeruginosa collected in several French ICUs.

Material & methods

• Between February and October 2009, 326 P. aeruginosa strains were collected from a multicenter prospective cohort study of patients hospitalized in several French ICUs (Dynapny Study).
• Isolates resistant to at least one carbapenem were included. The identities of the strains were confirmed by API strips and their susceptibilities to antibiotics by Liofilchem® PATHOGENIC SYSTEM AST (Liofilchem, Italy).
• After genotyping the strains by PFGE, clonal strains were excluded to avoid strains acquired through cross transmission.
• Imipenem, meropenem and doripenem MICs were determined by the Agar dilution method and by E-tests.
• In 25 representative strains, the mechanisms responsible for carbapenem resistance were determined by the KPC & MBL disc kit (Liofilchem, Italy) and molecular approaches (PCR).

Results

326 collected strains, 46 were resistant to carbapenem and included in the study (52% colonization/48% infection).

<table>
<thead>
<tr>
<th>MIC</th>
<th>n = 46 (%)</th>
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<tr>
<td></td>
<td>range</td>
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<tr>
<td>IMP</td>
<td>8 - 64</td>
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<tr>
<td>MRP</td>
<td>1 - 128</td>
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<tr>
<td>DOR</td>
<td>0.25 - 32</td>
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</tbody>
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Conclusion

The in vitro activities of doripenem and meropenem against carbapenem resistant P. aeruginosa were equivalent and better than imipenem activity. The genetic determinants responsible for resistance to carbapenems in the strains are multiple: hyper expression of AmpC, loss of porins and /efflux together with production of a KPC like carbapenemases. The molecular characterization of the strains is still ongoing.