pathway in anaerobic bacteria. However, nitazoxanide does not require nitroreduction to become active and has recently been postulated to affect PFOR activity at an earlier stage than metronidazole. This may explain why C. difficile strains with reduced susceptibility to metronidazole remain fully susceptible to nitazoxanide. Non-toxigenic C. difficile PCR ribotype 010 (metronidazole MIC 8–16 mg/L) was marginally less susceptible to nitazoxanide. Non-toxigenic C. difficile within the accepted variance of MIC studies.

In conclusion, nitazoxanide showed excellent activity against all C. difficile isolates tested in this study, regardless of metronidazole susceptibility or epidemic type. The results display the potential of nitazoxanide as a treatment option in CDI and highlight the value of further clinical assessment of this agent.

Funding
This study was supported by internal funding.

Transparency declarations
J. F. has received financial support to attend meetings from Bayer and Wyeth. S. D. B. has received financial support to attend meetings from Bayer and Targanta Therapeutics. M. H. W. has received honoraria for consultancy work, financial support to attend meetings and research funding from Astellas, Asto-Zeneca, Bayer, bioMérieux, Cerexa, Nabiriva, Novacta, Pfizer, Summit, The Medicines Company and Viropharma. S. L. T. and G. S. H.: none to declare.

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J Antimicrob Chemother 2011
doi:10.1093/jac/dkr078
Advance Access publication 3 March 2011

IMP metallo-β-lactamase-producing clinical isolates of Enterobacter cloacae in the UK

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Keywords: carbapenems, carbapenemases, Enterobacteriaceae

Sir,

Carbapenems, such as imipenem, meropenem and ertapenem, are often the main option for treatment of infections caused by multiresistant Gram-negative bacteria, particularly those that produce extended-spectrum or AmpC β-lactamase enzymes. However, the clinical utility of these antimicrobials is under threat with the emergence and spread of acquired genes coding for carbapenem-hydrolysing β-lactamases. These enzymes are broadly classified as serine carbapenemases (e.g. KPC) or metallo-carbapenemases (e.g. IMP, VIM and NDM), based on the hydrolytic mechanism at the active site.1

Ertapenem resistance in Enterobacter spp. is not uncommon and is mostly mediated by a combination of AmpC enzyme production and porin loss;2 imipenem and meropenem resistance is rarer, and more likely to be due to acquired carbapenemases. We report our experience with the first IMP metallo-β-lactamase-producing Enterobacter cloacae isolated from patients admitted to Addenbrooke’s Hospital.

In 2008–09, three isolates of meropenem-resistant E. cloacae were referred to the HPA Microbiology Services, Colindale, for confirmation. Two of these isolates were from blood cultures of haematology patients in an intensive care unit at the same time and one was from the urine of a renal transplant recipient. These isolates were resistant to gentamicin, tobramycin and tigecycline, and retained susceptibility only to amikacin and colistin. At the reference laboratory, the isolates were tested for carbapenem resistance by the BSAC agar dilution method3 and screened for carbapenemase production by the modified Hodge test.1 Carbapenemase genes were sought by PCR. PFGE of total DNA, digested with XbaI, was performed for strain comparison.

All three meropenem-resistant E. cloacae isolates showed potential of the activity of imipenem in the presence of EDTA, indicating that they produced metallo-carbapenemases, and gave positive modified Hodge test results. PCR revealed the carbapenemases to be IMP types. A 651 bp intragenic fragment, from nucleotides 47 to 697 of the 741 bp blaIMP allele, was sequenced from all three isolates. The predicted amino
acid sequences were identical to IMP-1 carbapenemase and, hence, different from other known IMP variants. PFGE showed that the three isolates belonged to a single strain; nevertheless, no epidemiological link was identified between the renal and haematology patients, or with hospitals elsewhere in the UK or overseas.

This is the first identification of *E. cloacae* with an IMP carbapenemase in the UK based on submissions to HPA Microbiology Services, Colindale. It is part of a pattern whereby carbapenemase production is becoming more widespread in the Enterobacteriaceae, though, generally, KPC, NDM and VIM enzymes are more frequent than IMP types.4–6 The emergence of carbapenemase-producing *Klebsiella* spp. clinical isolates from the UK.


References


**Acknowledgements**

We would like to express our gratitude to Dr David M. Livermore, at the HPA Microbiology Services, Colindale, for helpful discussions.

**Funding**

This work was supported by internal funding.

**Transparency declarations**

None to declare.