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 \textit{C. difficile} strains with reduced susceptibility to metronidazole remain fully susceptible to nitazoxanide. Non-toxigenic \textit{C. difficile} PCR ribotype 010 (metronidazole MIC 8–16 mg/L) was marginally less susceptible to nitazoxanide (0.5 mg/L) than the other isolates we examined, but this result is within the accepted variance of MIC studies.

In conclusion, nitazoxanide showed excellent activity against all \textit{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.

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**References**


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**IMP metallo-β-lactamase-producing clinical isolates of \textit{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.

Ertapenem resistance in \textit{Enterobacter} spp. is not uncommon and is mostly mediated by a combination of AmpC enzyme production and porin loss;\textsuperscript{7} 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 \textit{Enterobacter} cloacae isolated from patients admitted to Addenbrooke’s Hospital.

In 2008–09, three isolates of meropenem-resistant \textit{E. cloacae} were referred to the HPA Microbiology Services, Colindale, for confirmation. Two of three 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 ticarcillin and retained susceptibility only to amikacin and colistin. At the reference laboratory, the isolates were tested for carbapenem resistance by the BSAC agar dilution method\textsuperscript{4} and screened for carbapenemase production by the modified Hodge test.\textsuperscript{5} Carbapenemase genes were sought by PCR. PFGE of total DNA, digested with XbaI, was performed for strain comparison.

All three meropenem-resistant \textit{E. cloacae} isolates showed potentiation 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 \textit{bla}\textsubscript{IMP} allele, was sequenced from all three isolates. The predicted amino

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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.6–6 The emergence of carbapenemase-producing bacteria is a major public health concern. Producer strains should be actively sought to prevent their transmission among patients.

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References

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Trends in carbapenemase-producing Escherichia coli and Klebsiella spp. from Europe and the Americas: report from the SENTRY antimicrobial surveillance programme (2007–09)

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Keywords: carbapenem resistance, Enterobacteriaceae, KPC

Sir,
A large number of acquired carbapenemases have been identified and characterized among Gram-negative pathogens. These diverse enzymes, belonging to either molecular classes A and D (serine carbapenemases and oxacillinases) or molecular class B [metallo-\(\beta\)-lactamases (MBLs)], have emerged on a global scale and represent serious public health challenges, compromising therapeutic choices and complicating patient management.1–3 Genes encoding carbapenemases are associated with mobile genetic elements that allow rapid dissemination in the clinical setting. Therefore, detection and surveillance of carbapenemase-producing organisms have become matters of major importance for the selection of appropriate therapeutic schemes and the implementation of infection control measures.1–3

In this study, we analysed the rates of carbapenem resistance and carbapenemase production among a total of 15948 isolates of Escherichia coli (n = 10 432) and Klebsiella spp. (n = 5516) consecutively collected during 2007–09, which were evaluated as part of the SENTRY antimicrobial surveillance programme. E. coli and Klebsiella spp. were sampled from 83 medical centres located in the USA, Europe and Latin America (30, 10 and 43 institutions, respectively). These consecutive non-duplicate isolates were cultured from bloodstream, respiratory tract, and skin and skin structure infections. Isolates were tested for antimicrobial susceptibility using the 2009 CLSI broth microdilution method4 and results were interpreted according to the M100-S20-U document (CLSI, 2010).5 E. coli ATCC 25922 and Pseudomonas aeruginosa ATCC 27853 were concurrently tested for quality assurance; all results were in the CLSI published range.6

Overall, resistance to imipenem and/or meropenem (MIC values ≥2 mg/L) was observed among 2.0% (323/15948) of the E. coli (n = 29) and Klebsiella spp. (n = 294; 281 Klebsiella pneumoniae and 13 Klebsiella oxytoca) isolates (Table 1). All 323 isolates resistant to imipenem or meropenem were tested with the modified Hodge test (MHT)5 using imipenem and meropenem discs, and