Susceptibility of *Escherichia coli* and *Staphylococcus aureus* isolates from a district general hospital in the UK to tigecycline and other antimicrobials

E. CHIRISERI*, M. A. MINASSIAN* and R. O. JENKINS†

**Microbiology Laboratory, Northampton General Hospital, Cliftonville Road, Northampton NN5 6LF; and †Faculty of Health and Life Sciences, De Montfort University, The Gateway, Leicester LE1 9BH, UK*

The global prevalence of antimicrobial-resistant bacteria, including methicillin-resistant *Staphylococcus aureus* (MRSA) and extended-spectrum β-lactamase (ESBL)-producing *Escherichia coli*, cannot be underestimated. These multidrug-resistant phenotypes severely limit available therapeutic options, leading to morbidity, increased costs and extended hospitalisation.

This study reports on tigecycline activity, evaluated using Epsilometer test (Etest) strips, against contemporary ESBL-*E. coli* and MRSA isolates from a district general hospital in the UK. It also assesses susceptibilities of these isolates to a wide range of antibiotics, some of which are commonly used for the treatment of MRSA or ESBL-*E. coli* infections. These antimicrobial susceptibility patterns are compared to isolates of methicillin-sensitive *S. aureus* (MSSA) and isolates of non-ESBL *E. coli.*

In this study, bacterial isolates were obtained from samples collected from Northampton District General Hospital in-patients or out-patients from within Northamptonshire, UK; isolates were collected over the period January 2007 – March 2008. Only one isolate per patient was included in the study and duplicate isolates were excluded from the study. The isolates were recovered mainly from urine and wound swabs, and also respiratory or blood culture samples.

Presumptive identification of *E. coli* isolates was on chromogenic UTI agar plates (Oxoid). Cefpodoxime (10 μg disc) was used to differentiate ESBL- from non-ESBL *E. coli* isolates, with further identification and confirmation of ESBL phenotype using the Vitek-2 system. Presumptive *S. aureus* isolates on blood agar plates and chromogenic MRSA plates (Oxoid) were confirmed using a latex particle agglutination kit (Pro-Lab) and by inoculation on DNase agar plates (Oxoid). Confirmation of MRSA identification and assessment of antimicrobial susceptibility was by Vitek-2 analysis. *E. coli* ATCC 25922 and *S. aureus* ATCC 25213 were used as control strains.

Correspondence to: Professor R. O. Jenkins
Email: roj@dmu.ac.uk

Tigecycline Etest was carried out on confirmed ESBL-*E. coli* and MRSA isolates according to the manufacturer's instructions (AB Biodisk, Solna, Sweden). Using the cut-off established by the US Food and Drug Administration (FDA), all of the ESBL-*E. coli* isolates and 98% (49/50) of the MRSA isolates were susceptible to tigecycline; ESBL-*E. coli* isolates were inhibited at 1 μg/mL, while MRSA isolates were inhibited at 0.5 μg/mL. For ESBL-*E. coli* isolates, the Etest-determined minimum inhibitory concentration (MIC) values (Table 1) were generally consistent with those reported for Spain in 2006,[1] although a more recent study in Spain[2] has reported higher MIC_{90} and MIC range values, as determined by Etest. Upper MIC range values, determined by broth microdilution, in Canada,[3] the USA[4] and Taiwan[5] were two- to eight-fold higher than those determined by Etest in the present study. Conversely, for the Asia-Pacific rim region,[6] the MIC ranges determined by broth microdilution were lower than those obtained in the present study. For MRSA isolates, the MIC values obtained in the present study (Table 1) were generally consistent with values obtained in other recent studies from Europe and North America.[2,7,8] Non-susceptible MRSA isolates have been reported for the UK (1/50, 2%, Etest) in the present study, Turkey (2/14, 14.4%, Etest)[9] and the USA (3/2440, 0.1%, microbroth dilution).[10]

Comparison of Vitek-2 antibiotic susceptibility patterns for ESBL-*E. coli* (n=50) and non-ESBL *E. coli* (n=20) isolates showed greatly reduced susceptibility of the former group to the β-lactams (percentage susceptible in parentheses, ESBL:non-ESBL) amoxicillin-clavulanic acid (10:85), aztrionem (4:100), cefalotin (0:55), cefepime (6:100), cefotaxime (3:100), ceftazidime (0:100), cefuroxime (0:100), piperacillin (2:100) and cefaclor (3:100), with the exception of two carbapenem antibiotics – ertapenem and meropenem (100:100) and piperacillin/tazobactam (97:100). ESBL-*E. coli* also showed moderately reduced susceptibility to the aminoglycosides amikacin (43:100), gentamicin (66:95) and tobramycin (20:90); the quinolones nalidixic acid (14:85) and ciprofloxacin (19:95); and to nitrofurantoin (86:95) and trimethoprim (27:85).

Vitek-2 antibiotic susceptibility patterns for MRSA isolates showed 100% resistance to the β-lactams tested, ampicillin, amoxicillin-clavulanic acid, benzylpenicillin, ampicillin/sulbactam, oxacillin, imipenem, cefaclor, cefotaxime, ceftrioxime, cefuroxime and to the quinolone antibiotic ciprofloxacin. However, all MRSA isolates tested were 100% susceptible to each of the following antibiotics: the glycopeptides vancomycin and teicoplanin, the aminoglycoside gentamicin, the oxazolidinone linezolid, the

Table 1. Activity of tigecycline against ESBL-*E. coli* and MRSA isolates determined by Etest.

	Number	MIC_{50} (μg/mL)	MIC_{90} (μg/mL)	Range (μg/mL)	%susceptible	
ESBL-*E. coli*	50	0.25	0.38	0.094-1.0	100*	98†
MRSA	50	0.125	0.25	0.094-0.5	98*,†	

MIC_{50} and MIC_{90} are MICs for 50% and 90% susceptibility, respectively.

Tigecycline susceptibility breakpoints used were: *US FDA, ≤2 μg/mL for *E. coli*, ≤0.5 μg/mL for *S. aureus*; †EUCAST, <1 μg/mL for *E. coli*, ≤0.5 μg/mL for *S. aureus*.

MIC for ESBL-producing *E. coli* ATCC 25922 (control strain) was 0.5 μg/mL; MIC for *S. aureus* ATCC 25213 (control strain) was 0.125 μg/mL.

pristinamides combination quinupristin/dalfopristin, also rifampicin and chloramphenicol. In comparison with MSSA isolates (n=70), MRSA isolates showed decreased susceptibility (percentage susceptible in parentheses, MRSA:MSSA) to the macrolides erythromycin (26:79), azithromycin (20:83) and clarithromycin (26:90).

Several recent studies have verified the accuracy and utility of the Etest for determining bacterial susceptibility to tigecycline.[10] A paucity of data on tigecycline activity against UK isolates prompted this study. The results showed that tigecycline exhibited potent activity against ESBL-*E. coli* and MRSA isolates collected from a regional hospital in the UK during 2007–2008, as determined by Etest. Compared with previous studies on isolates from different countries/regions, where most determined tigecycline activity by microbroth dilution, there was no evidence to indicate a trend towards increasing tigecycline MIC values.

The results of the present study not only inform clinical decision-making within a district general hospital in the UK, but also serves as a timely monitor for the emergence of multidrug resistance. As tigecycline is utilised more widely, the involvement of clinical laboratories, using simple Etest and automated systems (e.g., Vitek-2), are likely to have an increasingly important role in monitoring trends in resistance on a local, national and global scale. Further study or surveillance is suggested to monitor the development of resistance to tigecycline and other antibiotics. Tigecycline has limited effectiveness in the treatment of urinary tract infection, which further highlights the need for alternative antibiotic therapy, as well as the need for new antibiotics in the future.

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The lactate gap revisited: variable interference with lactate analyses in ethylene glycol poisoning

M. P. CORNES*, C. FORD* and R. GAMA*†

**Department of Clinical Chemistry, New Cross Hospital, Wolverhampton; and †Research Institute, Healthcare Sciences, Wolverhampton University, Wolverhampton, West Midlands.*

Ethylene glycol poisoning may present with a profound metabolic acidosis due to an accumulation of its metabolites, glycolic acid and glyoxylic acid. Glycolic and glyoxylic acids, however, may or may not interfere in lactate assays based on lactate oxidase methods and therefore may give false high lactate results depending on the analytical platform used.[1–5] These metabolites, however, do not interfere in lactate dehydrogenase methods used for lactate measurement.[6] It has therefore been suggested that the presence of a 'lactate gap' when the same sample is analysed on different platforms is an indication of ethylene glycol poisoning,[1,5–9] allowing earlier initiation of treatment while awaiting definitive biochemical confirmation of ethylene glycol ingestion.[6]

The authors recently encountered a case of ethylene glycol poisoning where blood lactate measured on a Radiometer ABL 835 blood gas analyser in the accident and emergency department was disproportionately high compared to serum lactate measured on the central laboratory's Roche Modular analyser. Glycolic acid and glyoxylic acid interference in lactate assay on the Radiometer ABL 835 is well recognised.[1–3,6] There are, however, no data on possible interference from ethylene glycol metabolites in lactate assays performed on the widely used Roche Modular.

This study aims to assess the effects of glyoxylic and

Correspondence to: Dr Michael Cornes
Clinical Chemistry, New Cross Hospital, Wolverhampton WV10 0QP, UK
Email: michael.cornes@rwh-tr.nhs.uk