selected to have unique randomly amplified polymorphic DNA fingerprint patterns.

The antibiotic discs used (Table 1) were from HiMedia Lab. Ltd, India, except piperacillin, piperacillin/tazobactam, ceftriaxone/sulbactam (kindly provided by Ranbaxy Lab. Ltd, India) and imipenem, which were obtained from Oxoid, Basingstoke, UK. *E. coli* ATCC 25922, *E. coli* ATCC 35218 and *Klebsiella pneumoniae* ATCC 700603 were used as control strains. The results were interpreted as per the CLSI (formerly NCLLS) criteria, except for ceftriaxone/sulbactam. Because there are no published breakpoints for the latter combination, the susceptibility criterion used for this combination was >8 mm increase in zone diameter of ceftriaxone/sulbactam in comparison with that of ceftriaxone alone. Phenotypic ESBL detection by disc synergy tests was performed on all 54 isolates using co-amoxiclav and piperacillin/tazobactam discs as a source of inhibitors. Briefly, the test inoculum (equivalent in turbidity to that of a 0.5 McFarland standard) was streaked on Mueller–Hinton agar. Discs of co-amoxiclav (20/10 μg) or piperacillin/tazobactam were placed 20 and 30 mm, centre to centre, from discs containing cefotaxime (30 μg), ceftazidime (30 μg) and cefpirome (30 μg) and plates were incubated at 37°C overnight. Enhancements of zones of inhibition of cephalosporins towards piperacillin/tazobactam or co-amoxiclav were considered as positive ESBL results. All tests were performed in duplicate.

Comparative susceptibilities of the isolates against individual β-lactam antibiotics and β-lactam/β-lactamase inhibitor combinations are shown in Table 1. A total of 96.3% of isolates were susceptible to ceftriaxone/sulbactam in comparison with only 12.9% susceptible to piperacillin/tazobactam. This contrasts with previous international1 and national2 studies, which reported that combinations of β-lactam with tazobactam showed greater activity than β-lactam/sulbactam combinations against *E. coli* isolates. This marked difference may reflect different mechanisms in the different bacterial collections. In the present study, we specifically looked at CTX-M group-1 and CTX-M-15 producers and found ceftriaxone/sulbactam to be a highly effective combination (activity being equal to that of imipenem) in contrast to piperacillin/tazobactam and ticarcillin/clavulanate. Two isolates that were resistant to ceftriaxone/sulbactam were also resistant to imipenem (Table 1); they carried *blaCTX-M-15* and *blaAMPc* alleles (data not shown).

In disc synergy tests, none of the 54 ESBL producers was detected when co-amoxiclav discs were placed 30 mm from cephalosporin discs, and only 4 isolates (7.4%) were detected when this was reduced to 20 mm. It is known that optimal disc placement is an important issue in such tests. However, when piperacillin/tazobactam discs were used and the discs were placed 20 mm apart, we readily detected most ESBL-producing isolates; synergy with ceftriaxone, ceftazidime and ceftazidime allowed detection of 92.6% (50/54), 90.7% (49/54) and 74.1% (40/54) of ESBL producers, respectively. When the discs were placed at 30 mm, ESBL could still be detected in all the isolates; most (88.9% with ceftriaxone and 83.3% with cefotaxime) of the isolates still giving excellent synergistic patterns. On the basis of these findings, we feel that piperacillin/tazobactam (or tazobactam alone) could be a better indicator when combined with ceftriaxone and cefotaxime for the phenotypic detection of ESBLs, especially in CTX-M producers. This needs to be evaluated further and also against other classes of β-lactamases.

To conclude, ceftriaxone/sulbactam proved to be effective in vitro against 54 diverse CTX-M-15-producing *E. coli* strains. This novel combination merits further investigation, as does the use of piperacillin/tazobactam discs for the phenotypic detection of ESBLs.

**References**


**Correspondence**

Sir, *Candida albicans* and other emerging *Candida* spp. are a common cause of severe disseminated infections. Fluconazole has been traditionally used in the treatment of candidaemia. However, its activity against some species of *Candida*, such as *Candida krusei* and *Candida glabrata*, is very limited or even
In addition, emerging fluconazole resistance has been reported in species typically susceptible to this agent, such as *C. albicans*. The echinocandins have a different target from that of azoles, with potential both for additive effects with azoles and for activity against azole-resistant fungi. Micafungin is a new echinocandin with excellent *in vitro* and *in vivo* activities against *Candida* spp.

In this study, we hypothesized that the combination of fluconazole with micafungin could be advantageous over each monotherapy against *Candida* spp. and as the mechanisms of action of both drugs are different, antagonism might not be expected. Moreover, the use of antifungal combinations permits smaller doses, shorter duration of therapy and a wider spectrum of activity. Synergistic interactions between fluconazole and micafungin have already been observed in previous *in vitro* studies on *Cryptococcus* spp. and other basidiomycetous yeasts.

A total of 105 clinical isolates were tested (15 *C. albicans*, 20 *Candida dublindiensis*, 15 *C. glabrata*, 20 *C. krusei*, 10 *Candida lusitaniae*, 10 *Candida parapsilosis* and 15 *Candida tropicalis*). The isolates were subcultured on Sabouraud dextrose agar plates and incubated at 35°C for 24 h. Yeasts suspensions were adjusted to 1–5 × 10⁶ cfu/mL by counting with a haemocytometer. Micafungin (Astellas Pharma Inc., Tokyo, Japan) and fluconazole (Pfizer Inc., Madrid, Spain) were obtained as pure powders and diluted in sterile distilled water. Drug interactions were assessed by the checkerboard microdilution method [according to the CLSI (formerly NCCLS) M27-A2 document] and included the MIC determinations of each drug alone. The MIC was defined as the lowest concentration that produced 50% growth inhibition (

<table>
<thead>
<tr>
<th>Candida species (number of isolates)</th>
<th>MIC-2 (mg/L)*</th>
<th>Percentage of isolates showing the following interactions</th>
<th>FICI, range</th>
<th>MIC</th>
<th>FLC</th>
<th>MFG</th>
<th>FLC/MFG</th>
<th>A, I, S</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>C. albicans</em> (15)</td>
<td>0.87</td>
<td>&lt;0.5 to &gt;32</td>
<td>0.25</td>
<td>0.25</td>
<td>0.15</td>
<td>1.67</td>
<td>16.13</td>
<td>0</td>
</tr>
<tr>
<td><em>C. dublindiensis</em> (20)</td>
<td>0.27</td>
<td>&lt;0.5 to &gt;32</td>
<td>0.38</td>
<td>0.62</td>
<td>0.12</td>
<td>0.25</td>
<td>8.30</td>
<td>0</td>
</tr>
<tr>
<td><em>C. glabrata</em> (15)</td>
<td>6.65</td>
<td>0.5 to &gt;32</td>
<td>1.33</td>
<td>1.33</td>
<td>0.13</td>
<td>10.07</td>
<td>8.30</td>
<td>0</td>
</tr>
<tr>
<td><em>C. krusei</em> (15)</td>
<td>47.8</td>
<td>16 to 102</td>
<td>1.53</td>
<td>1.53</td>
<td>1.53</td>
<td>1.00</td>
<td>8.30</td>
<td>0</td>
</tr>
<tr>
<td><em>C. lusitaniae</em> (10)</td>
<td>0.61</td>
<td>&lt;0.5 to &gt;2</td>
<td>12.13</td>
<td>12.13</td>
<td>0.61</td>
<td>0.53</td>
<td>8.30</td>
<td>0</td>
</tr>
<tr>
<td><em>C. parapsilosis</em> (10)</td>
<td>1.57</td>
<td>&lt;0.5 to &gt;32</td>
<td>0.16</td>
<td>0.16</td>
<td>0.16</td>
<td>0.53</td>
<td>8.30</td>
<td>0</td>
</tr>
<tr>
<td><em>C. tropicalis</em> (15)</td>
<td>1.57</td>
<td>&lt;0.5 to &gt;32</td>
<td>0.16</td>
<td>0.16</td>
<td>0.16</td>
<td>0.53</td>
<td>8.30</td>
<td>0</td>
</tr>
</tbody>
</table>

FLC, fluconazole; MFG, micafungin; GM, geometric mean; S, synergism; I, indifference; A, antagonism.

*MIC-2, the lowest concentration that produced 50% growth inhibition.*
when this drug was combined with fluconazole. This combination could be of interest in those cases where the isolates of this species show high MICs of fluconazole. In spite of the predominance of indifferent interactions, which agrees with the results provided by other authors, the lack of antagonism and the percentages of synergism obtained against C. albicans and C. tropicalis are interesting issues. Although scarce in vivo data on the activity of this combination are available, it has been demonstrated that it was able to prolong survival and to reduce tissue burden in murine models of C. glabrata infection and in trichosporonosis. Therefore, combination of these agents may warrant future clinical evaluation in Candida infections.

Acknowledgements
This work was supported by a grant from Fondo de Investigaciones Sanitarias from the Ministerio de Sanidad y Consumo of Spain (PI 050031).

Transparency declarations
None to declare.

References

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Journal of Antimicrobial Chemotherapy
doi:10.1093/jac/dkm114
Advance Access publication 21 April 2007

Travel-acquired salmonellosis due to Salmonella Kentucky resistant to ciprofloxacin, ceftriaxone and co-trimoxazole and associated with treatment failure
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Keywords: extended-spectrum cephalosporins, Clostridium difficile, gastroenteritis

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Sir,
In Belgium, the vast majority of salmonellosis is caused by the serovars Enteritidis and Typhimurium, which represent together more than 80% of the isolates. Salmonella enterica serovar Kentucky is a very uncommon serovar that represented 0.02% to 0.5% of the total isolates during the last decade, but 0.8% in 2006. Indeed, this serovar showed a usual increase in Europe during the third quarter of 2006 with several of them acquired during travels to Northeast Africa and Turkey. We report here the first Belgian case of a travel-acquired multidrug-resistant Salmonella Kentucky resulting in a treatment failure because of a high resistance level to ciprofloxacin and secondarily acquired resistances to extended-spectrum cephalosporins (ESCs) and trimethoprim+sulfamethoxazole (co-trimoxazole).

In September 2005, a 77-year-old healthy man on a cruise along the North Africa coast developed febrile diarrhoea a few hours after a meal (chicken couscous and dates) in a small restaurant on the Libyan coast. Consequently, he was admitted for 48 h in a hospital in Cairo (Egypt) and treated with intravenous (iv) mezlocillin followed by co-trimoxazole given orally for a few more days whereby he slowly recovered.

Two weeks after his return to Belgium, he presented again with febrile diarrhoea and arthritis of the wrist. After examination of his stool, the Clostridium difficile stool toxin test was positive and Salmonella Kentucky was isolated. The Salmonella isolate